ON OPSONIN:

AND THE

OPSONIC INDEX

IN THE

TUBERCULIN (T. R.) TREATMENT

OF

PULMONARY TUBERCULOSIS

BY

JAMES MILLER, M.B. et C.M. (1891).

19th, April, 1906.

.....

PART 1.

INTRODUCTORY and METHODS:

CHARACTERS and MODE of ACTION

of OPSONIN.

.....

In 1897 Denys made comparative tests of the phagocytic action of different sera . He charged tubes containing leucocytes, with measured quantities of emulsion of strepto-:cocci, and to some of these tubes added immune serum, and to others normal serum. By plating loopfuls taken from these tubes at various periods, and counting the colonies, he was able to demonstrate a marked diminution of living streptococci in the tubes containing immune serum, but an increase in the tubes containing normal serum. He found that the leucocyte of the immunised animal was not more active as a phagocyte than the leucocyte of the normal animal. The difference in the two cases was entirely due to a property of the serum.

Mennes, in the same year, using the same method of experimentation with pneumococus,

obtained similar results to those arrived at by Denys with streptococcus.

The results of these two workers are open to the criticism of Metchnikoff, that the occurrence of a certain amount of agglutination with immune serum would appear to give a diminution in the number of the colonies.

The honour of the first recorded attempt to make a direct quantitative estimation of the phagocytic power of the leucocytes of the blood must, I think, be accorded Major W. B. Leishman, M.B. et C.M. (Glasg.), R.A. M.C., at the time Assistant Professor of Pathology, Army Medical School, Netley. Having before him the recent work of Professor Wright and others on the estimation of the bactericidal power of the blood fluids, and the extremely feeble power which these fluid constituents had been shown to possess for the destruction of such organisms as the common staphylococcus pyogenes and the bacilli of anthrax and plague, he set about devising a method whereby the phagocytic action of the leucocytes of the blood could be measured.

Briefly his method aims at enumerating the bacilli or cocci ingested within a definite time by the polynuclear cells of the blood under examination, obtaining an average of these values, and comparing the result with that of a control blood placed under identical conditions. The steps in the process are as follows. An emulsion of a portion of a fresh agar culture of the germ whose action is to be investigated is made in a few drops of normal saline solution in a watch-glass, a well-marked but not too dense opacity being aimed at. A well-polished microscope slide and two perfectly clean cover-glasses are prepared. A small capillary pipette fitted with an indiarubber teat is taken in hand and a mark placed upon it at a suitable dis-:tance from the point according to the volume of blood and emulsion desired. From a needle prick in the finger one volume of blood is drawn into the capillary pipette, a bubble of air allowed to enter, and then an equal volume of emulsion of germs; these are well mixed by blowing on to a clean watch-glass and drawing out and into the pipette several times. A drop of the mixture is placed upon

one end of the clean slide and a cover glass placed over it. A precisely similar preparation is made of the control blood and a drop placed upon the opposite end of the slide. The slide is next placed in a moist chamber and put into an incubator at 37 C. for half an hour. At the end of that time the slide and cover glasses are separated by moistening the dried margins with normal saline solution and gently sliding apart as in makingblood films. By staining the films upon the slide, both the control and experimental film are stained by one operation. The films are rapidly dried in the incubator and then fixed and stained by Leishman's modification of Romanovski's stain, dried in the air without heat, and examined with an oil-immersion lens. The number of germs in 20 polynuclear leucocytes is then counted in each film, the polynuclears being taken as they come in view, only those which are manifestly broken being neglected.

To use Leishman's own words the method is obviously very far removed from being an ideal one; the dilution of the blood with salt solution, the variation in the number, and possibly in the virulence of the germs introduced, and, perhaps, the variation of the

phagocytic power of the control blood from day to day, are a few of the more obvious objections; but the identical conditions to which the blood under examination and the control blood are submitted at least partially annul the effects of variations due to differences in the number and the virulence of the germs. (Leishman, Brit. Med. Jour., Jan. 11, 1902.)

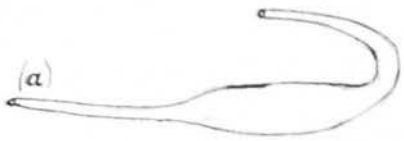
Modifications of Leishman's method introduced by Professor A.E.Wright and Captain Stewart R. Douglas.-- These modifications consisted in (a) conducting the phagocytosis in capillary tubes, making films afterwards, and (b) using citrate of soda in normal saline solution to prevent coagulation of the blood and so being free from the complications introduced by clotting.

Having conducted their investigations into the bactericidal action of the blood fluids in capillary pipettes, it would naturally occur to Professor Wright and Captain S.R. Douglas to impress these into Leishman's method. Their first procedure was to take a capillary pipette fitted with a rubber teat, put a mark upon the stem and to aspirate into it one volume

of blood from the finger, one volume of a one per cent solution of citrate of soda in physiological salt solution, and one volume of a bacterial suspension made by shaking up a twenty-four-hours agar culture in physiolog-:ical salt solution and centrifugalising in order to remove bacterial clumps. The three equal volumes were mixed together by blowing out upon a clean slide and re-aspirating several times in succession. A portion of the mixture was drawn into the capillary tube of a pipette, the orifice of the tube sealed in the flame of a Bunsen burner, and the pipette placed in an incubator at 37 C. for fifteen minutes. The pipette was then removed, the tip broken off and a film made of the contents, and stained with Leishman's dye. As a bacterial suspension of 10,000,000,000 to the cubic centimetre was used, very high phagocytic counts would be obtained.

The next procedure recorded by Wright and Douglas was employed to "elicit separately the role of the white corpuscles and the blood fluids in phagocytosis". Here again they impressed into use apparatus of previous investigations. Into a definite quantity

of citrate of soda physiological salt solution in a blood capsule such as is here figured, was received an equal quantity of blood from the finger.



Having rarified by heat the air in the capsule the end (a) was sealed up in the flame. The contents, thus withdrawn from the syphon-neck into the capsule, were shaken up to mix thoroughly and centrifugalised. The citrated plasma was pipetted off and preserved, and the remaining corpuscles well-washed and centrifugal-:ised three times with physiological salt solu-:tion. Citrated serum was also prepared by allowing blood to clot and mixing the expressed serum with an equal volume of the citrated soda solution. In the way set forth were obtained citrated plasma, citrated serum, and washed white blood corpuscles. Comparative experiments of the action of the citrated plasma and the citrated serum in phagocytosis of staphlylococci were carried out by Wright and Douglas, who came to the conclusion that there was no difference in their action quantitatively. Having arrived at this con-:clusion they used in their further experiments

ordinary (uncitrated) serum.

The next series of comparative experiments were conducted with unheated, and heated, serum the latter being raised to a temperature of 60° to 65° C. for ten to fifteen minutes and then cooled. In these experiments they showed that in mixtures containing staphylococci, polymorphonuclear corpuscles, and serum which had not been heated, phagocytosis was very active; whereas in a similar mixture but with heated serum substituted for unheated serum, phagocytosis was very much reduced. They therefore concluded that an important role must be ascribed to the blood fluids in phagocytosis. The residuum of phagocytosis with heated serum, and also with the normal serum incubated with bacteria and heated, does not receive any explanation by Wright and Douglas.

In a further series of experiments in which staphylococci and unheated serum were incubated at 37 C. for fifteen minutes, then exposed for ten minutes to a temperature of 60 C., cooled, and again incubated with washed white blood corpuscles, they showed that phagocytosis was still active, although when

the serum was heated before the cocci were exposed to its action, phagocytosis was almost nil. They therefore further concluded that the serum had a direct action on the bacteria, modifying them in such a way as to render them an easy prey to the phagocytes, and spoke of this action as an "opsonic" effect, and employed the word "opsonins" to designate the elements in the blood fluids whcih produced this effect. Wright and Douglas- Proceedings of the Royal Society, Vol. 72, 483, Oct. 31st. 1902.

Later, Wright and Douglas undertook exper-:iments with a view to determining whether the increased phagocytic effect obtained with un-:heated serum was, in the case of tubercle bacilli, due to an action exerted by the serum directly upon the tubercle bacilli. The following is taken from the record of these experiments.

EXPERIMENT 1.

S.R.Ds unheated serum ----------2 vols
A.E.Ws washed corpuscles ----------2 vols
suspension of heated tubercle bacilli---1 vol.
Phagocytic index (average of 20 P.W.B.C) 6.9

(B)

S.R.Ds unheated serum ----------2 vols
Suspension of heated tubercle bacilli --1 vol.
The above were digested for fifteen minutes at 37 C., were then heated to 60 C. for ten minutes, and finally three volumes of the mixture were added to
A.E.Ws washed corpuscles ----------2 vols
Phagocytic index (average of 31 P.W.B.C) 3.5

(C)

S.R.Ds unheated serum----------2 vols
Suspension of heated tubercle bacilli---1 vol.
The above were immediately, after mixture, heated to 60 C. for ten minutes and were then added to
A.E.Ws washed corpuscles ----------2 vols.
Phagocytic index (average of 50 P.W.B.C) 0.16.
They concluded from these, and many similar experiments, that the serum acted directly upon the tubercle bacilli and they called this action an "opsonic" action. They further stated that the smaller phagocytic effect recorded in each experiment in (B) as compared with (A) is at present without explanation. I shall refer to this point later.
Wright and Douglas, Proceedings of the Royal Society vol. 74, Sept. 28, 1904.

REFERENCES.

Denys 1897. "Resultats obtenus par le serum Antistreptococcique", International Medical Congress at Moscow, Section 3, p. 82.

Mennes (1897). Zeitschrift fur Hygiene, vol. 25. p. 413.

Leishman. Brit. Med. Jour., Jany. 11, 1902.

Wright and Douglas Proceedings of the Royal Society, vol. 72, No. 483, Oct. 31, 1903.

Wright and Douglas. Proceedings of the Royal Society, vol. 74, Sept, 28, 1904.

After they adopted and modified the method suggested by Leishman the following is a brief description of the very beautiful technique arrived at by Wright and Douglas for the study of phagocytosis and its quantitative estimation, as gathered from their publications. It will be seen that the requisite apparatus is of a very simple character.

APPARATUS.

1. Glass capsules for collecting blood, of capacity to hold about 0.2 c.c.
2. Two tubes about 6 or 8 millimeters in diameter and 5 cm. in length, in which to wash the white blood corpuscles.
3. Small square glass troughs or watch-glasses with 2 cover glasses, in which to put the washed white corpuscles.
4. Capillary tubes about 14 to 16 cm. long and of the calibre of those used for collecting and storing calf lymph.
5. Several capillary-pointed pipettes with rubber teats.
6. Two or three large sized pipettes with teats to correspond.
7. Two or three conical flasks (Erlenmeyer's) in which tokeep sterile solutions for use.
8. An agate mortar and pestle.
9. A good supply of large flat corks (bungs)

perforated to hold the blod capsules upright, each cork appropriately labelled.

10. Cover-glasses (No. 1.), slides, and forceps.

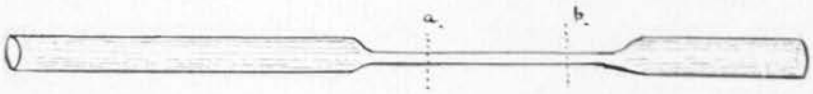
11. A rack capable of holding one or two dozen cover-glasses for staining purposes; or where films are made directly on the slides, a rack to hold a similar number of slides.

12. Two solutions are required, one solution containing 0.85 % sodium chloride, and another containing 0.85 % sodium chloride and 1 % sodium citrate.

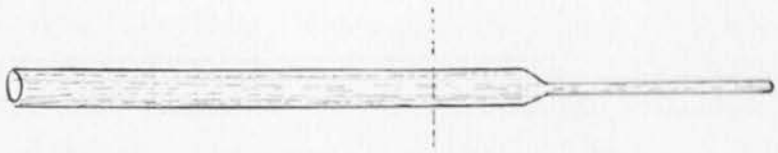
The articles enumerated 1,2,4,5,6, can be readily prepared in any laboratory where a good blow-pipe is at hand. Take a piece of glass -tubing about 12 cm. long and 6 to 8 mm in diameter, dry thoroughly and heat the middle portion in the flame of the blow-pipe; draw it out slightly and break through at the constriction with the aid of a file, seal up the narrow ends and we have got two tubes each about 5 or 6 cm long.

The glass capsules are made ofthe same kind and size of glass-tubing and at the same time the capillary tubes are made. Take a piece of tubing about 20 or 30 cm. long and heat it about 3 or 4 cm. from one end in the blow-pipe flame. When thoroughly softened draw out to a fine

capillary tube, and in a small flame seal off at the point (a) and (b).

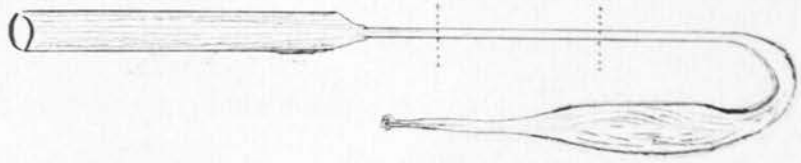


We have then (1) a piece of glass for making a capillary-pointed pipette, (2) a capillary tube which can be kept sealed and sterile until wanted for use, and (3) tubing drawn out at one end ready for making blood capsules and more capillary tubes. Out of this piece of tubing about 30 blood capsules can be made in the following way.



The blow-pipe is again essential and the tube is heated in the position of the dotted line a little over 1 cm. from the constriction in the drawing so as to get a capsule about 1 cm. long in its widest part. When soft, the glass is drawn out and, while keeping the capillary tube straight, the right hand containing the capsule is turned downwards so as to give the capsule a curved neck, which is very useful when it comes to filling with blood by syphon

action, and when centrifugalising.



The capillary tube is again sealed at the dotted lines, and in each operation we now obtain a sealed sterile capsule and a sealed sterile capillary tube.

The piece of tubing for making the capillary-pointed pipette is next taken in hand. The finer portion is warmed in a peep-light and when soft is quickly drawn out to a fine capillary point, sufficiently fine to be easily inserted inside the capillary tubes already made; a rubber teat is fixed at the opposite end and the capillary-pointed pipette is ready for use. It is advisable to keep at least half a dozen such pipettes at hand as the points are very easily broken. This piece of appartaus is the ingenious device of Ian Struthers Stewart M.D. (Edin.).

The larger-sized pipettes are made from tubing about 1.5 cm. or more in diameter. These pipettes are used for drawing off the supernatent fluid after washing and centrifugalising the white corpuscles, and transferring the latter to a watch-glass. They are also useful for measuring and transferring small quantities of the saline solutions.

METHODS OF PROCEDURE.

1. Collection of blood. From each patient whose blood is to be examined, and also from a healthy person whose blood is to be taken as a standard of comparison, some blood is collected in capsules in the following way. Either the lobe of the ear is pricked, or the patient can be instructed to collect his own blood from the finger. The hand is allowed to hang down for a few minutes so that the fingers become filled with blood. A bandage or handkerchief is now wound round from the root of the finger to the terminal inter-phalangeal joint, and the engorged finger is pricked with a sterile pricker, just above the root of the nail, when an abundant supply of blood will be obtained. The sealed ends of a capsule having been been broken off, the capsule is inverted and its curved end applied to the drop of blood until it is about two-thirds full. The ligature is then removed from the finger when the bleeding instantly ceases. The empty end of the capsule is warmed in the flame of the spirit lamp to rarify the air, care being taken not to burn the blood, and when warmed the point is sealed. As cooling and contraction of the enclosed air takes place rapidly, the blood is withdrawn from

the curved neck which is then also sealed. As each capsule is filled it is either labelled or enclosed in an envelope with the name of the person written thereon. All the necessary bloods havingbeen collected, they are allowed to clot and then centrifugalised, the clotting being hastened by placing in the incubator at 37 C. for a short time. After being centrifugalised each capsule, the neck snipped off with bome forceps, is placed upright on an appropriately labelled cork.

2. Preparation of washed white corpuscles.

Take the two small tubes and fill to a depth of three centimetres with saline citrate solution (1 % sodium citrate and 0.85 % sodium chloride). Collect into each tube blood to the depth of an additional centimetre, preferably from the ear of a healthy person, after having cleansed the part with alcohol. Shake frequently so as to well-mix the blood and saline citrate solution to prevent coagulation. The two tubes are centri-:fugalised thoroughly and the clear fluid containing the blood plasma is pipetted off. The remaining corpuscles are now shaken up with 0.85 % solution of sodium chloride only and again centrifugalised, the clear fluid drawn off and the layer of washed white corpuscles transferred by a pipette to a

covered watch glass. It has been found that it is quite immaterial to the result whether the washed white corpuscles are derived from the blood of a healthy person or from the patient himself.

3. Preparation of emulsion of tubercle bacilli.

The agate mortar and pestle are thoroughly cleansed of all antiseptic, usually lysol, in which they are kept. About 10 milligrams of dried sterile tubercle bacilli are dropped into the mortar and rubbed down to a fine powder; about 0.5 c.c. of normal saline solution is added from a pipette, the whole being well-triturated to form an emulsion with which a capsule is filled and sealed in the usual way. The emulsion is centrifugalised to throw down all masses, leaving only a fine suspension of tubercle bacilli. The neck is snipped off and the capsule placed upright on its appropriate cork. So that it may be readily distinguished it is well to have a perforated rubber bung to hold the capsule containing the emulsion of tubercle bacilli.

The next step consists in making a mixture of equal volumes of washed white corpuscles, serum, and emulsion of tubercle bacilli, for incubation, beginning with the control or standard

which is prepared with the serum from healthy normal blood. First select a capillary tube and break off the sealed end. Holding it against the palmar aspect of the left index finger, place a mark upon it with an oil pencil, about one inch from its finer extremity. Into the other end fit a capillary pipette, and squeeze the teat between the thumb and forefinger to expel the air. Now aspirate the preparation of white blood corpuscles into the capillary tube up to the pencil mark and then draw in a bubble of air, after which take up the same measured quantity of serum from the healthy normal blood and again an air bubble, and lastly aspirate a similar quantity of emulsion of tubercle bacilli. In the capillary tube there are now three equal volumes, one of white corpuscles, one of serum, and one of emulsion of tubercle bacilli separated by bubbles of air; these are expelled on to the slide by squeezing the collapsible teat, they are thoroughly mixed and again aspirated into the capillary tube, which is now sealed at both ends, labelled, and put into the incubator at 37 C. for 20 minutes. The serum from each patient's blood is similarly treated, a record being kept on the glass-door of the incubator of the order in which the tubes

are put in and the time at which they have to be taken out. When the 20 minutes have passed each tube is taken out, the ends snipped off , and its contents blown out upon a cover-glass, and a film made by using the capillary tube to spread the contents over the cover-glass. Where a large number of observations has to be made, one may save the trouble of cleaning and mounting cover-glasses by makingthe films directly upon *this* slides. The films are fixed by drying in the incubator, when they are all stained together. By the use of a miniature photographic rack a large number of films can be stained at one time, a rack with a sufficient number of grooves to carry two dozen cover-glasses being a very convenient size. The cover-glasses are held down by a clip and the whole placed in a capsule of hot carbol-fuchsin warmed over a water-bath. Dilute sulphuric acid of strength 1 % is used for declourising, for the reasons that we know we are dealing with only one form of bacillus and also because the dried sterilised tubercle bacilli are more easily deprived of their stain than tubercle bacilli, say, from sputum. As a counter-stain Delafield's haematoxylin, or polychrome methylene blue may be used. The films are dried, and mounted in

xylol balsam in the usual way.

The above methods are largely those elaborated by Wright and Douglas, except in slight details, and in the method of fixing and staining, and in preparing large numbers of specimens at one time .

COUNTING THE INGESTED TUBERCLE BACILLI IN THE PREPARED BLOOD FILM.

For this purpose 1/12th inch oil-immersion objective and a good light-- critical light-- are indispensible. Unless a good light is available bacilli contained within, or otherwise obscured by, the nuclei of the polynuclear cells may be over looked. The ingested bacilli in the first thirty consecutive polymorphonuclear cells are counted, this type of cell being regarded as most active in the destruction of pathogenic organisms, the action of all other leucocytes being disregarded. The count obtained from the enumeration of ingested bacilli in the case of a healthy serum is taken as the standard or control, and for purposes of comparison is regarded as unity. The ratio of the phagocytic count in the test film to that of the control being regarded as the Opsonic Index, or the measurement of the power of resistance (in this case to the tubercle bacillus) of the tuberculous subject compared

with the power of resistance (to the tubercle bacillus) of a normal healthy person taken as unity. Thus, suppose in the case of the healthy serum we obtain a phagocytic count of 46, and in the case of serum from a person suffering from tuberculosis we obtain a count of 14, the Opsonic Index of the tuberculous individual would be expressed as follows, 46: 14:: 1: 0.3, or shortly Opsonic Index--14/46--0.3.

In the work of enumerating the ingested bacilli it very soon becomes evident that one worker cannot check the actual enumerations of another, for, even if the second individual goes over the same parts of the slide, in the large majority of instances his enumerations will vary by a very appreciable amount from those of the first person. This occurrs even after long practice in counting ingested bacilli. My only explanation for this variability is that the personal factor enters largely into this matter of enumeration. In a few instances two workers may obtain the same number when they separately count a slide, but when a bacillus is enclosed in a well-stained nucleus it may be readily overlooked where the power of vision is not very sharp. The attempt, therefore, of two workers to arrive at the same enumeration in all cases

is found to be very discouraging. However, when the personal factor has been recognised and each worker counts the control- film, and each test-film for himself, dividing the count of the latter in each instance by the number of ingested bacilli in the control, the results are wonderfully uniform and are quite comparable, not varying by more than 0.1 in a few instances. It is a mistake then in a division of labour for one worker to count the control-film while another counts the test-film because uniform results will not be arrived at; each worker must make his own count of the control-film, and divide each of his counts of test-films by his own control count.

CHARACTERS and MODE of ACTION of OPSONIN.

Before entering upon a discussion of the characters of the substance in the serum named opsonin and its mode of action, I will briefly refer to the work of several authors bearing more directly upon this particular subject-- work of course entirely based upon the theories of Metchnikoff and Ehrlich.

Bordet holds that a specific bactericidal serum contains a thermostable substance, "substance sensibilisatrice"-- which acts upon the micro-organisms and prepars them for the thermo-labile alexine, of proteolytic ferment, which acts as the solvent. He compares the action of immune serum to that of a mordant. In certain cases, however, such as in streptococcus infection, the bactericidal action is slight, and in such cases he attributes to the immune serum a stimulating action on the leucocytes. The leucocytes and other cells can perceive the presence of a prevent-:ive serum, and under its stimulus they are capable of reacting by movement. They manifest towards the immune serum a pronounced positive chemiotaxis.

Bordet. 1895. Annales de l'Institut Pasteur. vol 9 p.462.

Bordet 1897. " " " Vol. 11, p. 177.

Sawtchenko and Melkich come to the conclusion that the immune substance, or "fixateur", acts as an intermediate body between the microorganisms and the leucocyte, transforming the negative chemiotaxis of the leucocyte into a positive chemiotaxis. At a later date Sawtchenko, chiefly by experiments on the phagocytosis of red blood corpuscles, corroborated this view. He holds therefore that the immune substance fully merits Ehrlich's designation of intermediary body (Zwischenkorper).

Sawtchenko and Melkich 1901. Annal de l'Institut Pasteur. Vol. 15, p. 498.

Sawtchenko 1902. " " " Vol. 16.p.106.

Levaditi showed by experiments in vitro, that the cholera vibrios were ingested by the polynuclear leucocytes of the peritoneal exudate of a normal guinea-pig,and that the intracellular vibrios were converted into granules (Pfeiffer's phenomenon, intracellular), whereas the extracellular organisms remained unaltered. From a series of experiments he came to the conclusion that this result was due to the presence of immune body-- "substance sensibilisatrice"-- in sufficient quantity to enable phagocytosis to occur, the complement for

the intracellular change of the vibrios into a globular form being supplied from the leucocyte itself. On the other hand extracellular solution of the microbes did not take place owing to a lack of complement. Levaditi also showed that the vibrios on to which the "substance sensibilis-:atrice" had been fixed, when introduced into the circulation of a normal animal were rapidly englobed by phagocytes, just as they are in the case of an actively immunised animal. The extra-phagocytic conversion of the vibrios into granular form doesnot take place if sufficient precautions are observed to avoid injury to the leucocytes. Levaditi 1901. Annales de l'Institut Pasteur Vol .15, p. 894.

Wright and Douglas, as already quoted, find that there is present in normal blood serum a substance which, unaided, prepares the bacilli so that they are capable of ingestion by the leucocytes, and have introduced the terms "opsonin" and "opsonic effect" to designate the substance and its action. They find that the opsonin is destroyed if heated to a temperature of 60° C. for ten minutes, and that the leucocyte is an indifferent factor in the matter, merely ingesting the micro-organisms which have been prepared for it.

As a result of inoculation of bacterial vaccines, the amount of opsonin present in the blood may be increased.

Wright and Douglas 1902. Proceedings of the Royal Society Vol. 72, p. 357.

Wright and Douglas, ibid. vol. 74. p. 159.

Bulloch and Atkin have confirmed the observ-:ations of Wright and Douglas. They find that the opsonin disappears from the serum when the latter is mixed with bacteria; and that the opsonin is destroyed, not merely converted into a "non-opsonising" modification, by the action of heat. They further state that it is a simple body, and is not identical with any of the anti-bodies hitherto discovered in the serum.

Bulloch and Atkin 1905. Proceedings of the Royal Society, Vol. 74. p. 379.

Neufeld and Rimpau find that the immune sera, in the case of streptococcus and pneumo-:cocccus, act on and change the micro-organisms so that they are secondarily taken up by the leucocytes. They find that the substance which produces this effect is thermostable.

Neufeld and Rimpau 1904. Deutsche Medizinische Wochenschrift. Jahrgang 30, p. 1458.

Hektoen and Ruedgier confirm most of Wright and Douglas' results. In opposition to Bölloch and Atkin they conclude that opsonin has a complex constitution, there being present a haptophorus group, which fixes on the microbe, and an opsinophorus group, which produces a physical or chemical change in the microbe.

Hektoen and Ruediger 1905. "Studies in phago-:cytosis." Journal of Infectious Diseases. Vol.2, p. 128.

Dean, in a communication to the Royal Society, came to the conclusion, contrary to Wright and Douglas and others, that opsonin and the substance -- "fixateur" or "substance sensibilisatrice"-- in immune serum were identical and were not destroyed by heating to 60 C. And therefore that the term opsonin seeing no new substance had been demonstrated in the serum, should be retained only to designate a property of immune serum.

Dean 1905. Proceedings of the Royal Society, Vol. 76, p. 506.

REFERENCES.

Bordet 1895. "Les Leucocytes et les Proprietes Actives du Serum ches les Vaccines." Annales de l'Institut Pasteur. Vol. 9.p.462.

Bordet 1897. "Contribution a l'Etude de Serum Antistreptococcique." Annales de l'Institut Pasteur. Vol. 11, p. 177.

Sawtchenko and Melkich 1901. "Etude sur l'Immunite dans le Fievre recurrent." Annales de l'Institut Pasteur Vol. 15, p. 459.

Sawtchenko 1902. "Du Role des Immunesines (Fixateurs) dans le Phagocytose." Annales de l'Institut Pasteur. Vol.16, p. 106.

Levaditi 1901. "Sur l'Etat de la Cytase dans le Plasma des Animaux normaux et des Organisme Vaccines contre le Vibrion Cholerique." Annales de l'Institut Pasteur. Vol. 15, p. 894.

Wright and Douglas 1903. "An experimental Investigation of the Role of the Blood Fluids in connection with Phagocytosis". Roy. Soc. Proc. Vol. 72, p. 357.

Wright and Douglas 1904. "On the action exerted upon the Tubercle Bacillus by the Human Blood Fluids" Roy. Soc. Proc. Vol.74, p. 159.

Bulloch and Atkin 1905. "Experiments on the Nature of the Opsonic Action of the Blood Serum". Roy. Soc. Proc. Vol. 74. p. 379.

Neufeld and Rimpau 1904. "Uber die Antikorper des Streptokokken-und Pneumokokken-Immunserums." Deutsche Medizinische Wochenschrift. Jahrgang 30, p. 1458.

Hektoen and Ruediger 1905. "Studies in Phagocytosis" Journal of Infectious Diseases, Vol .2 p.128.

Dean 1905. "On the Nature of the Substance in Serum which influences Phagocytosis". Roy. Soc. Proc. Vol. 76, series B. p. 506.

The following observations were made and conclusions arrived at before becoming acquainted with the results of the work of Neufeld and Rimpau or of that of Dean, and I venture to set forth an account of some of my experiments as probably helping to elucidate further the character and mode of action of the substance termed "opsonin" in normal serum, or in serum possessing a low degree of immunity.

In remarking upon their experiments (quoted on pages 9 and 10) Wright and Douglas state that the smaller phagocytic effect in each experiment in B, as compared with A, is at present without explanation. The observations following offer, I think, a satisfactory explan-:ation of this difference. In experiments on serum from the blood of a healthy robust man in whom the phagocytic index for tubercle bacilli was high, as measured by Wright and Douglas' modification of Leishman's method, it has been found on many occasions that the phagocytic index obtained with serum which had been heated to 60° c. for ten minutes was considerably higher than that obtained with the unheated serum. In the following cases the normal serum index is taken as unity.

Experiment 1.

1. volume of washed corpuscles

1 volume heated serum

1 volume emulsion of tubercle bacilli

mixed and incubated at 37 C. for 20 minutes.

Phagocytic index-- 1.4.

Experiment 2.

1 volume washed corpuscles

1 volume heated serum

1 volume emulsion of tubercle bacilli

mixed and incubated at 37 C. for 20 minutes .

Phagocytic index-- 1.7.

Experiment 3.

1 volume washed corpuscles

1 volume serum heated for 20 minutes at 60 C.

and cooled

1 volume emulsion of tubercle bacilli

mixed and incubated at 37 C. for 20 minutes.

Phagocytic index--1.4.

Experiment 4.

1 volume washed corpuscles

1 volume serum heated for 30 minutes at 60 C.

and cooled

1 volume emulsion of tubercle bacilli

mixed and incubated at 37 C. for 20 minutes.

Phagocytic index---0.9.

Experiment 5.

The serum in this instance was obtained from a case of 4 lobed lesion of the lungs. The unheated serum gave a phagocytic index of 1, compared with the healthy control as unity.

1 volume washed corpuscles

1 volume serum heated for 10 minutes at 60 C. and cooled

1 volume emulsion of tubercle bacilli

mixed and incubated at 37 C. for 20 minutes

Phagocytic index--1.7.

After heating at 60 C. for 30 minutes the same serum gave an index of 0.6.

Such results as the foregoing appear at first sight to be subversive to previous ideas arrived at after perusal of Wright and Douglas' papers upon the action of heated serum. Certainly, this result of a higher index with heated than with unheated normal serum was obtained in a small number of observations--in the majority of observations, in fact as a rule, the phagocytic index with heated serum is lower than with the same serum unheated. But even a limited number of such observations requires ex-:planation, as also does the occurrence of

phagocytosis to any degree with serum which has been subjected to a temperature of 60 C. for any length of time. It occurred to me that normal serum containes substances which are not equally resistant to heat--in fact, that there is some substance resembling comple-:ment (required for the bactericidal action of a serum with a high degree of immunity) which is easily destroyed by the action of heat; and also that there is another substance resemb-:ling immune body which is more resistant to the action of heat. The complement-like body is furnished by the white corpusclesof the blood. On heating the serum to 60 C. all this complement-like substance in the serum is destroyed so that when again mixed with normal white corpuscles a state of unstable equilibrium exists. At a suitable temperature, namely 37 C. there is therefore an increased positive chemio-taxis between the heated serum and the poly-nuclear white corpuscles, the amount of positive chemiotaxis depending upon the quantity of immune body contained in the heated serum. The result of this action is shown under the microscope by the increased numbers of tubercle bacilli ingested by polynuclear cells.

The following experiments would seem to lend support to this view. In these experiments the phagocytic index of the normal unheated serum is taken as the standard or unity.

First. the serum is heated at 60 C. for 10 minutes.

Experiment 1. The phagocytic index of the heated serum is taken and as a rule it is found to be below unity, although, as in instances quoted it may be above unity.

Second, normal washed blood corpuscles are treated with heated serum. They are mixed in equal volumes and incubated for 20 minutes at 37°C. The mixture is then centrifugalised so as again to separate the corpuscles from the serum--these corpuscles, well-washed in normal saline solution, being known in the following record of experiments as "treated washed corpuscles" and this serum as "treated heated serum".

Experiment 2. 1 volume of heated serum, 1 volume of treated washed corpuscles, and 1 volume of tubercle bacilli emulsion are mixed and incubated and the phagocytic index obtained.

Experiment 3. 1 volume normal unheated serum, 1 volume treated washed corpuscles, and 1 volume of tubercle bacilli emulsion are mixed and incubated, and the phagocytic index obtained.

Experiment 4. 1 volume treated heated serum, 1 volume normal washed corpuscles, and 1 volume tubercle bacilli emulsion are mixed and incubated and the phagocytic index obtained .

Experiment 5. 1 volume normal unheated serum 1 volume tubercle bacilli emulsion are mixed and incubated for 20 minutes at 37 C. Subsequently this mixture is heated at 60 C. for 10 minutes, cooled, and 2 volumes added to 1 volume of treated washed corpuscles and again incubated at 37 C. for 20 minutes and the phagocytic index obtained.

The following series of experiments A.B.C.D. show some of the results arrived at.

A.

1. Heated serum
Normal washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--0.6

...

2. Heated serum
Treated washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--0.0

...

4. Treated heated serum
Normal washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--1.6

...

B.

1. Heated serum
Normal washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--0.7

...

3. Normal unheated serum
Treated washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--0.26.

...

4. Treated heated serum
Normal washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--1.06.

...

C.

1. Heated serum
Normal washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--0.9

...

2. Heated serum
Treated washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--0.09.

...

3. Normal unheated serum
Treated washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--0.45.

...

4. Treated heated serum
Normal washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--0.8

...

D.

In this series of experiments the serum was heated to a temperature of 62 C. for 10 minutes and then cooled.

1. Heated serum
Normal washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--1.13.

...

2. Heated serum
Treated washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--0.00

...

3. Normal unheated serum
Treated washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--0.66.

...

In this film (3) the bacilli were for the most part collected round the polynuclear cells, lying end on to the cell but not inside it.

4. Treated heated serum
Normal washed corpuscles
Tubercle bacilli emulsion
Phagocytic index--1.6.

...

5. 1 volume normal serum
1 volume of tubercle bacilli emulsion
mixed and incubated at 37 C for 20 minutes. Subsequently heated at 62. C for 10 minutes, cooled, and 2 volumes of the mixture added to

1 volume treated washed corpuscles
Phagocytic index (60 cells)--0.00

...

Those sera with which a higher phagocytic index was obtained in the heated than in the unheated condition were from the blood of healthy individuals whose power of resistance to the tubercle bacillus, as measured in this way, was normally high. In any case of serum heated for 10 minutes to 62 degrees Centigrade there is usually more or less residuum of phagocytic power when mixed with normal polynuclear white blood corpuscles and bacilli. This residuum of phagocytosis as shown in the foregoing experiments would seem to depend, for one factor, upon something contained in the polymorphonuclear cells. When these cells have been digested for 20 minutes at blood temperature with heated serum and again incubated with another portion of heated serum and an emulsion of bacilli, it is found that the power of phagocytosis is practically annhilated. In the subsequent films the cells are found to remain intact, the nuclei staining clearly in the usual way, but although bacilli are freely distributed through the films no phagocytosis has taken place. That the cells are not destroyed of injured is proved by experiment 3 where the requisite substances for phagocytosis are supplied in the serum.

These experiments show (1st) that there are two substances essential to an opsonic effect upon tubercle bacilli: (2nd) that one of these substances (resembling complement, cytase, or alexine, requisite for the bactericidal action of immune serum) is more thermolabile than the other (which may be looked upon as representing immune body), as witness the reduction in opsonic power when a serum is heated either before or after being allowed to act upon bacilli and then incubated with normal washed corpuscles: (3rd) that this complement-like substance is entirely destroyed by heating for 10 minutes at 60° Centigrade as witness experiments 2, and 5 D: and (4th) that this particular substance can be extracted, so to speak, from the polymorphonuclear cells, leaving these cells exhausted, and (the complement-like substance) in a condition still available for assisting in the preparation of bacilli for phagocytosis as shown in experiment 4. I have also performed the exper-:iment of adding normal serum to a heated serum in equal volumes with the result that the phagocytic index of the mixture was raised practically to that of the unheated serum.

By the experiments of Pfeiffer, Bordet, and others it has been demonstrated that in anti-bacterial sera the complement or cytase is more easily destroyed by heat, readily at 65 degrees Centigrade, and even by half-an-hour at 55°Centigrade, than the immune body.
Pfeiffer. Zeitschr.f.Hyg. XVlll.1; XX.198.
Bordet. Ann. de l'Inst. Pasteur lX. 462; Xl. 106.
Ehrlich and Morgenroth also showed that the immune body and complement entered into combination, the combination taking place most readily at a temperature of 37 Centigrade .
Muir and Ritchie 1902. pp. 462-464.
Ehrlich and Morgenroth. Berl. klin. Wchnschr. (1899), XXXVl. 6, 481; (1900), XXXVll, 453 681; (1901), XXXVlll, 251, 569, 598.

By the exposure of serum in these exper-:iments to a temperature of 60 C. for 10 minutes, 20 minutes, or 30 minutes, one must conclude that all the complement has been destroyed. The only available source of complement in the first experiment with heated serum is the white corpuscles themselves. The white corpuscles in thatcase must become the centre of any chemical action or combination which may take place, and also, since complement

in the serum is destroyed, any combination which does take place must in thatase be most active in and around the polynuclear corpuscles. Experiments 2 and 3 in the series A.B.C. and in experiment 5 D. show that somethinghas been extracted from the polynuclear cells which is an essential factor in phagocytosis. Experiment 4 indicates that the substance extracted from the corpuscles by heated serum is still available for preparing the bacilli for phagocytosis.

The view of the workers of the French school that an essential element in phagocytosis is derived from the leucocytes would seem to be borne out by these experiments.

Bordet. Ann. de l'Inst. Pasteur, Xll. 688, Xlll. 225, 273; XlV. 257; Xv. 303.

Muir and Ritchie. Manual of Bacteriology 1902. pp. 462 et subseq.

Neufeld and Rimpau announce, as a new discovery, a third variety of specific serum requiring a direct cellular intervention to complete the bactericidal effect, but no reference is made to the work of Wright and Douglas. Their results in a measure confirm those of Wright and Douglas, but contrary to

to these workers, Bulloch and Atkin, and others, Neufeld and Rimpau find "that the opsonic substance in the serum is not destroyed at a temperature of 60 C. and from this fact they argue that the opsonin comes into the category of an amboceptor which they think is complemented in the body of the leucocyte. They could not demonstrate that the serum had any stimulating effect upon the leucocyte, as maintained by Metchnikoff, and in this they are in agreement with Wright"
Bulloch. The Practitioner. Nov. 1905.

In my opinion the serum does not exert a stimulating effect upon the leucocytes, but that the leucocytes supply to the serum a substance which is readily destroyed by heat and without which the serum cannot exert its opsonic effect. Further, that this easily thermolabile substance furnished by the leuco-:cytes is normally present in the serum in amount varying with the quantity of the more thermostable (immune-body-like) substance which the serum contains, and that there is a state of equilibrium (or weak chemical union) main-:tained between the two, and, that as the more thermostable substance is increased, so is the

thermolabile substance increased. Also, that the thermostable substance--opsonin-- comes under Ehrlich's classification of receptor of the second order, or amboceptor and that it requires to be complemented before its action becomes evident; in other words, whether amboceptor or not, it requires the aid of another substance for its complete action and in this respect resembles immune body.

At a later date Wright and Reid acting upon a suggestion of their fellow-worker, Douglas, entered into an investigation of the action of the salt content of its fluid environment upon the activity of the leuco-:cyte. They found that, in certain concen-:trations of salt solution, the leucocytes displayed a considerable amount of (what they term) spontaneous phagocytosis, the maximum phagocytosis being displayed in a mixture of salt solution, washed corpuscles and tubercle bacilli which contained 0.56 % sodium chloride. At a concentration of 1.2 % sodium chloride in the mixture the phagocytosis reached a figure "which does not differ sensibly from zero". In these experiments with the higher concentration of salt solution the physico-chemical conditions

are so altered and so foreign to the leuco-:cyte that a reduction in phagocytosis is a foregone conclusion. Bearing upon this may be quoted the experiments of Barratt (Brit. Med. Journ., Jan. 20, 1906) upon the action of fluids of different densities upon chemiotaxis with paramoecia; also experiments quoted by Metchinikoff in his book on Immunity in Infectious Diseases.

Wright and Reid's experiments do not in any way disprove that the leucocytes yield something to heated serum which is essential to phagocytic action, but merely that, by a concentration of salt solution considerably above normal, positive chemiotaxis is held in abeyance. It is also conceivable that high concentrations of salt solution environment would prevent the diffusion of complement or cytase from the leucocyte into its surrounding medium.

REFERENCES.

Pfeiffer. Zeitschr. fur Hyg. XVlll. 1; XX. 198.

Bordet. Ann. de l'Inst Pasteur. lX. 462; Xl. 106.

Ehrlich and Morgenroth. Berl. klin. Wchnschr. (1899) XXXVl. 6; 481; (1900) XXXVll. 453, 681; (1901) XXXVlll. 251, 569, 598.

Bordet. Ann. de l'Inst. Pasteur. Xll. 688; Xlll. 225, 273; XlV. 257; XV. 303.

Muir and Ritchie. Manual of Bacteriology (1902) Pp. 462 et subseq.

Wright and Reid. Roy. Soc. Proc. Vol. 77. Series B.

Barratt. Brit, Med. Journ. Jany. 20th, 1906.

Metchnikoff. "Immunity in Infectious Diseases" (English translation) pp. 19. 31.

.....

PART 2.

THE TUBERCULO-OPSONIC INDEX in DIAGNOSIS,

and

TUBERCULIN (T.R.) AS AN AID IN THE TREATMENT OF

PULMONARY TUBERCULOSIS.

.....

The use of Tuber culin (T.R.) cannot be said to have passed entirely out of the experi-:mental stage. In other words although a very large amount of work has been done, there has not been collected a corresponding amount of data to guide one in the use of tuberculin in the treatment of tuberculosis. No doubt this is largely due to the discredit thrown upon the treatment by the disappointing results obtained in the use of the crude preparation originally introduced by Koch, and yet there is no doubt that Koch's method of treatment is on truly scientific lines. It is also to be remembered that the early praparation of tuber-:culin was tried on many unsuitable cases, pyrexial and others. The best field for the use of that first tuberculin is to be found in the reliable assistance if gives in the diagnosis of tuberculosis in cattle; but the use of any preparation of tuberculin in

sufficient dose to produce a temperature reaction in the human subject, I venture to think, cannot be entirely free from injurious action. Some method, therefore, had to be devised whereby a reaction not perceptible in temperature or pulse could be demonstrated and if possible measured. Indeed a reaction which looked at from the usual clinical standpoint, may be so slight as to have no effect upon the temperature or pulse, yet may be so profound as to be very detrimental to the patient. In the examination of the blood by Wright and Douglas' modification of Leishman's method-- in other words by the estimation of the opsonic index-- we have such a means of measuring a reaction not perceptible in pulse or temperature. The manner in which the method has been evolved, from the quantitative estimation of the phago-:cytic index and the use of staphylococcus vaccines, to the use of tubercle vaccines in minute doses, may almost be looked upon as a natural evolution.

For convenience, what follows will be divided into two parts. First, the opsonic index and tuberculin as an aid in diagnosis; and second, tuberculin as an aid to treatment in pulmonary tuberculosis.

THE OPSONIC INDEX and TUBERCULIN as an AID in DIAGNOSIS.

In comparing the phagocytic indices, which have been estimated under corresponding conditions, of a number of persons in health and reducing them to a standard of unity, it is found that there is not any great variation from that standard. The amount of variation of the phagocytic index consistent with health has been found to be limited to 0.2 above or below the standard. The largest series of deter-:minations of the opsonic content of the serum of healthy persons, the test material being tubercle bacilli, has been made by Bulloch (The Practitioner. Nov. 1905). He found in the case of 34 medical students and 32 hospital nurses that the tuberculo-opsonic index varied from a minimum of 0.8 to a maximum of 1.2 compared with that of the investigator himself taken as 1. Lawson and Stewart (Medico-Chirurg-:ical Transactions Vol. 89) in the case of 25 healthy individuals, chiefly living in the country found that the tuberculo-opsonic content of the blood serum varied from a minimum of 0.9 to a maximum of 1.2. In my investigation into the tuberculo-opsonic content of the serum in 30 healthy persons I find myself in agreement

with Bulloch that the healthy tuber culo-opsonic index may vary from a minimum of 0.8 to a maximum of 1.2. It is interesting to note that in three of this number, who gave a tuberculo-opsonic index of 0.8 after having lived in the town for many years, gave an index of 1.0 after six months residence in the country. From these observations therefore it is evident that a tuber culo-opsonic index as low as 0.8, or as high as 1.2, is consistent with freedom from tuber culous disease. The converse, however, that a person whose blood gives a tuberculo-opsonic index within these limits is therefore free from tuberculous disease, does not hold. As we shall see from the following tables many persons with tuberculous lesions give opsonic indices within these limits; but by making a series of observations upon the blood of a healthyperson and upon the blood of a person suffering from tuber culous disease marked differences will be found.

TABLE SHOWING THE DIFFERENCE IN OPSONIC CONTENT OF THE BLOOD SERUM IN A SERIES OF OBSERVATIONS UPON A HEALTHY PERSON, AND A PERSON SUFFERING FROM PULMONARY TUBERCULOSIS.

DAY.	HEALTHY PERSON.	PERSON SUFFERING FROM PULMONARY LESION.
1.	1.243	0.8
3.	1.2	1.1
5.	1.1$\dot{8}$	0.5
6.	1.185	0.5
7.	1.23	1.6
8.	1.18	0.8
9.	1.1	0.8
10.	1.1$\dot{6}$	2.3
12.	1.2	1.5
13.	1.19	1.3

The two series of indices are calculated to the same control. It will be observed from this table that in the case of the healthy individual the opsonic index is practically uniform throughout the series of observations extending over a fortnight. The average of the whole series works out to 1.1868. Allowing for experimental error, and error of

observation, the opsonic index of this healthy individual, for all practical purposes, may be taken as 1.2. From these and many other similar observations I conclude that the tuberculo-opsonic index in health is practically a uniform figure. On the other hand the opsonic index of the subject of a tubsculous pulmonary lesion is very unsteady taken over a corresponding period. Four out of the ten observations give an index within normal limits, but any one of the remaining six observations is indicative of tuberculosis, while the whole series could only be obtained from the blood of a person with tuberculous disease. This particular series of observations was obtained from a case of pulmonary tuberculosis undergoing Sanatorial treatment but not tuberculin treat-:ment.

The next series of observations shows the effect of small doses of tuberculin on the opsonic index of a person free from tubercle. The observations were made daily and form a consecutive series. For convenience the opsonic index is given to one place in decimals, the nearest figure at one place being taken as the index, e.g., the figures work out 0.875, or 0.823, the former is taken as 0.9, the latter as 0.8.

Before inoculation.	1/1000 mg. Tuberculin.
0.8	1.0
0.9	1.0
1.0	1.2
0.9	1.3
0.8	1.3
0.8	1.3
0.9	1.7
0.9	2.2
0.9	1.0
1/2000 mg. tuberculin	1.2
1.0	1.3
1.3	1.4
1.1	1.1
1.2	1.2
1.0	0.9
0.9	1/750 mg. tuberculin.
1.0	2.0
1.2	1.7
1.2	1.4
1.1	1.1
1.0	1.3
1.3	1.1
1.0	0.9
1.1	1.1
0.8	1.3
	1.2

In these tabulated figures there is a uniformity of results. The opsonic index taken for nine days before inoculation is practically steady. After the 9th observation, 1/2000th mg. tuberculin was administered and the observations continued, a higher index being the result. The third column shows the results after a dose of 1/1000th mg. tuberculin, followed in the fourth column by the results of a dose 1/750th mg. tuberculin. In this individual, who is free from tuberculosis,

the effect of tuberculin as administered was to increase the phagocytic index obtained with his serum. Careful watch was made for any symptoms or physical signs which might arise from the inoculations. None falls to be recorded. No depression followed by a feeling of exhilaration was felt after any dose, sensations which many patients state they have experienced after a dose of tuberculin. Although the opsonic index rose to above 2, the blood does not long contain this amount of opsonin, in a few days the index returning approximately to the ordinary level of health. The net result then of a small dose of tuberculin (T.R.) in a healthy subject is an increase of the phago-:cytic index. In three other healthy subjects the result of inoculation of a small dose of tuberculin was to raise the opsonic index to over 2 inall the cases, although in only one of these was a series of observations made, which is practically similar to the series given.

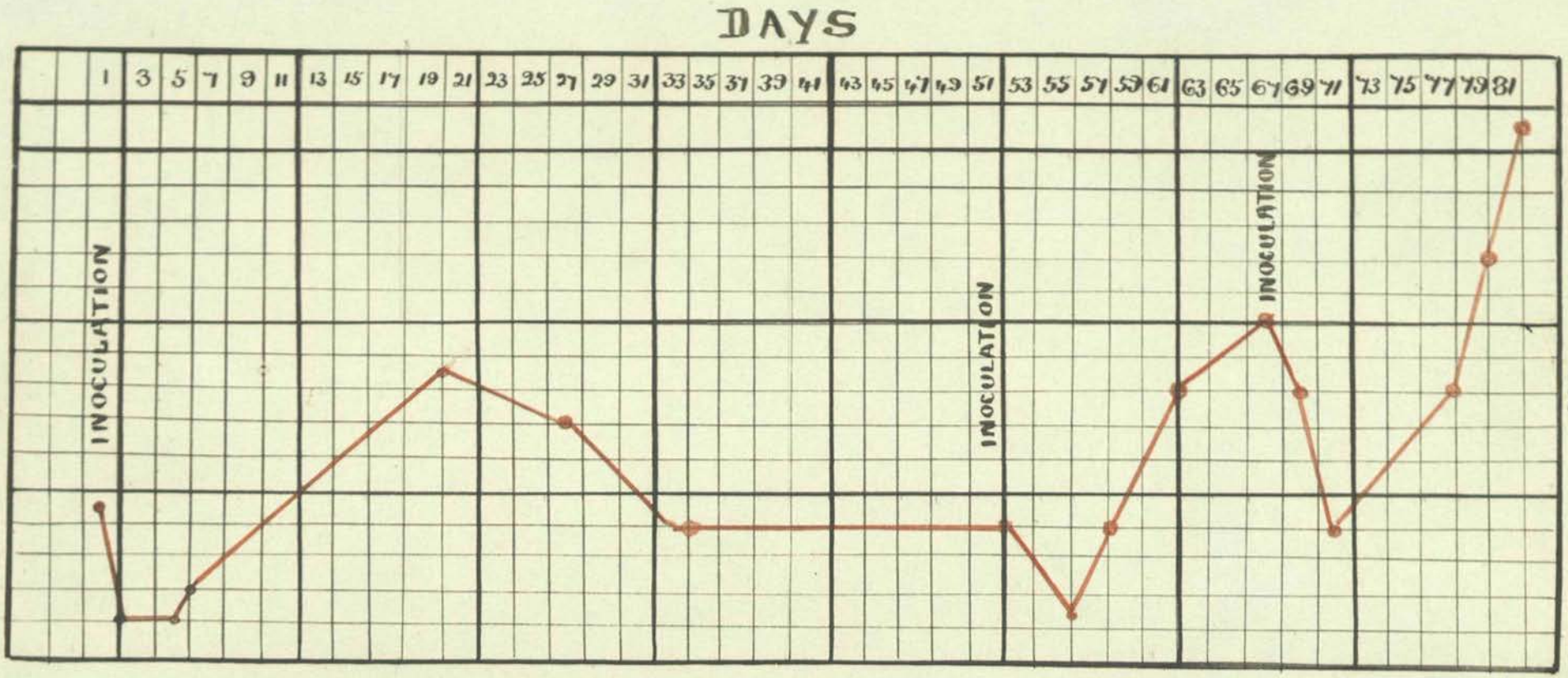
The next consideration is the effect of a dose of tuberculin upon a tuberculous subject.

Observations before and after inoculation with 1/2000th mg. Tuberculin (T.R.)

Day.	Opsonic Index.
1.	1.0
2.	0.9
6.	0.8
7.	0.9
8.	1.5
9.	1.5
12.	0.9
13.	0.6
14.	0.7
15.	0.8
16.	1.2
17.	1.5
19.	1.3
20.	1.5
21.	1.9
22.	1.3
26.	1.1
27.	1.0
28.	0.7
29.	0.8
30.	1.1
31.	1.2
33.	1.2
34.	1.3
35.	1.1
36.	1.2
37.	0.8
39.	0.7
40.	1.1
41.	1.0
42.	0.9
43.	0.7
45.	0.9
47.	1.2

The figures in red ink denote the observations preceeding inoculation.

First, as in the previous instance the opsonic indices are taken for a number of days before inoculation. In their irregularity these indices are typical of a tuberculous


DAYS
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 41 43 45 47 49 51 53 55 57 59 61 63 65 67 69 71 73 75 77 79 81
INOCULATION
INOCULATION
INOCULATION

subject. The seventh observation was found to give an opsonic index of 0.9, and on the evening of the same day a dose of 1/2000th mg. tuberculin was injected intra-muscularly. The opsonic index taken on the following day, twelve hours after inoculation, was found to have fallen to 0,6 an index lower than any previously recorded. After this initial fall there is a gradual rise with no fluctuations for several days. When the summit of the rise is reached the fall begins and the fluctuations, observable in the index before inoculation, again set in.

The course of events after the inoculation of a bacterial poison were first pointed out by Ehrlich and Brieger in connection with inoculations of tetanus toxin undertaken upon a milk goat which had been previously immunised. The accompanying immunity curve, taken from their paper, shows the tetanus antitoxin content of the milk at different intervals after inoculation (Zeitschrift fur Hygiene, Vol. XIII). Immediately after inoculation there is a fall in the antitoxin content of the milk, the fall being followed after two or three days by a steady rise, and then a gradual decline till

a point is reached a little above that at which the animal was inoculated. The same sequence of events follows each inoculation, the only difference being that the antitoxin content of the milk reaches a higher level after each inoculation. Similar results have been recorded by Salomonsen and Madsen (Ann. de l'Inst. Pasteur 1887) in connection with inoculations of diphtheria toxin.

Wright has characterised these phases of the curve of immunity as the "negative phase", the "positive phase" and the "higher base line".

In the case of inoculation of the tuber-:culous subject with tuberculin the first two phases are evident. There is the marked fall in the opsonic index on the day after inoculation followed by a gradual rise until on the third day, in the instance given, the negative phase is found to be over, and the positive phase has begun. This result is in accordance with Ehrlich's immunity curve in so far as there is a negative, followed by a positive phase; but it is in marked contrast with what follows the same or even a larger dose of tuberculin in a healthy subject. In the healthy subject the dose given produces no negative phase at all,

the organism being competent to deal with the amount of tuberculin toxin administered which seems at once to stimulate to activity the immunity-producing mechanism. The dose is apparently too small to produce a negative phase, for, from the experience of the immunis-:ation of animals one must conclude that if the dose administered were large enough a negative phase must follow. Why then should a negative phase follow the inoculation of an almost infinitesimal dose in the tuberculous subject and not in the healthy subject?. The only explanation is that the tuberculous subject has already within his organism a considerable amount of tubercle toxin which, when reinforced by the toxin of tuberculin injected, is sufficient to produce a negative phase. When, therefore, a negative phase in the opsonic index is obtained upon inoculation with very minute doses of tuberculin we may conclude that we have evidence of tubercle infection. This diagnostic point was also noted by Lawson and Stewart, although they offered no explanation of it, neither was a series of observations carried out after inoculation of a healthy subject(Medico-Chirurgical Soc. Proc. Vol. 89).

The only drawback to the very small dose of tuberculin as a diagnostic is that with such a small dose as 1/2000th or 1/1000th mg. the negative phase is sometimes, although very rarely in the first instance, elided in a tuberculous subject, and for diagnostic purposes a larger dose may have to be administered. Reference to the tables of opsonic indices which follow will show the frequency of the occurrence of the negative phase after inoculat-:ion even after tuberculin treatment has been carried on for a considerable time. We have here therefore, two valuable diagnostic points for the presence of tubercle; first, the irregularity of the opsonic index or a persist-:ently low or very high opsonic index before inoculation with tuberculin, and second, the negative phase following upon the inoculation of tuberculin in small doses.

TUBERCULIN as an AID in the TREATMENT of PULMONARY TUBERCULOSIS.

In this table the opsonic indices of two persons suffering from pulmonary tuberculosis are placed side by side, one undergoing tuberculin treatment, the other not.

DAY.	Non-Tuberculin Case.	Tuberculin Case.
1.	1.1	1.0
2.	1.0	0.8
3.	1.0	0.7
4.	0.8	0.7
5.	0.5	0.8
6.	0.6	1.2
8.	0.7	1.3
9.	0.8	1.3
10.	1.0	0.9
11.	0.6	0.5
12.	1.2	1.0
13.	---	1.4

While in the non-tuberculin case the opsonic index is a most variable factor, in suitable case for tuberculin treatment, after inoculation the course of the opsonic index might almost be predicted. The small dose of tuberculin seems to remove the numerous fluctuations and after the negative phase is over, produces a steady rise in the phagocytic power, first approximating to and then exceeding the phago-:cytic power in health. This increase however is not of long duration, the duration varying

greatly in different cases, the small dose of tuberculin having to be repaated again and again at suitable intervals indicated by the opsonic index from day to day, in order to stimulate the immunising-mechanism into activity.

In all casestreated with tuberculin the opsonic index was observed for several days before inoculations were begun, and it is certainly the most satisfactory course to continue the daily observations during the treatment. Cases have occurred in which the vagaries of the opsonic index were the first indication of extension of the disease, an example of which is case No. 19 which is recorded later. During the daily observations the plan adopted has been to re-inoculate when the decline in the phagocytic power of the positive phase has again set in, in order if possible to keep the phagocytic power at or above the normal in health. Inoculations with varying doses have also been undertaken, doses varying from 1/500th mg. to 1/2000th mg. tuberculin (T.R.), in order to find out if possible what dose has the maximum therapeutic effect. In the follo wing tables the dose

given, unless otherwise recorded, was 1/1000th mg. at first; after the 130th day the dose administered was 1/2000th mg. The chief difference to be noted is that with the smaller dose the number of negative phases is decreased, the immediate positive phases in the cases observed being in the majority. Up to the present however, it cannot be said that this point is of assistance in arriving at a prognosis.

In the following tables I have set forth the tuberculo-opsonic indices of a number of cases, the observations extending over a period of many months. For a short time the number of daily observations had to be greatly reduced on account of the severe strain upon the eyes entailed in the microscopic work. During the period in question some 3000 observations of tuberculo-opsonic indices were made. The following is a list of some of the cases with the diagnosis made in each instance, every available means including screening and X-ray photographs, being used to insure accuracy in diagnosis. The terms pyrexial and apyrexial refer to the time during which tuberculin treatment was carried on.

Case No.1 Early infiltration, right apical lesion with a history of bronchitis.

Case No. 2. Unilateral sub-acute disease (right side) with haemorrhages from time to time.

Case No.3 Bilateral chronic fibro-caseous disease (cavity) settling to fibroid; apyrexial.

Case No4. Chronic progressive disease,4 lobed lesion. Complications, malaria and pleurisy; apyrexial.

Case No. 5. Fibro-caseous disease, bilateral, 4 lobed lesion; pyrexial.

Case No.6 Right upper and lower lobes infiltrated; always pyrexia at menstrual periods, otherwise apyrexial.

Case No.7 Sub-acute disease tending to fibroid; apyrexial.

Case No.8 Early infiltration, right upper and doubtful very early lower lobe; apyrexial

Case No.9 Chronic fibroid disease, complicated with extensive laryngeal disease; apyrexial.

Case No 10. Left-sided disease, infiltration--complicated with chronic bronchitis and emphysema; pyrexial.

Case No.11 Sub-acute bilateral disease, 3 lobes involved; apyrexial.

Case No.12. Unilateral disease, 2 lobes. Mixed infection.

Case No.13. Chronic disease of 8 years standing 3 lobes affected, left upper and lower with early right upper lobe.

Case No.14. Fibro-caseous disease, 5 lobes involved: excavation present in both lobes on left side.

Case No.15 Early infiltration right upper and lower lobes.

Case No. 16. Early infiltration, right apex.

Case No.17 Early infiltration, fibroid in character; apyrexial.

Case No. 18 Unilateral chronic fibroid with numerous excavations; apyrexial. Inchio-rectal abscess operated upon and healed in 3 weeks.

Case No .19. Early infiltration. Right apex cleared up and left apex became involved and ischio-rectal abscess developed at the same time; apyrexial.

In the accompanying tables of these cases those indices typewritten and underlined in red ink denote the observations immediately preceeding an inoculation, the following observation being taken twelve to fifteen hours after inoculation. An underline alone, in red ink,

denotes an inoculation made without observation, a period of about ten to fifteen days being allowed to elapse between inoculations.

Days.

Case No.	Sex.	1.	3.	4.	5.	6.	7.	8.
1.	Female	0.9	1.4	0.8	1.0	0.8	1.0	1.0
2.	Male.	0.9	1.3	1.0	1.0	1.0	0.7	1.4
3.	Male.	1.1	1.4	1.1	0.7	1.1	0.9	1.1
4.	Male.	---	---	---	---	---	---	---
5.	Female	0.6	0.2	---	1.0	1.0	0.9	0.7
6.	Female	0.8	1.4	0.8	0.8	1.2	0.9	0.8
7.	Male.	0.9	1.5	1.4	1.0	1.6	1.3	1.3
8.	Male.	0.9	1.2	0.9	1.3	1.3	0.6	1.0
9.	Male.	0.7	0.9	0.9	0.7	1.3	0.9	0.8
10.	Male.	0.9	---	0.5	0.7	0.4	0.5	1.0
11.	Male.	0.5	0.9	0.7	0.6	0.8	0.6	1.0
12.	Male.	---	---	---	0.8	0.8	1.2	0.9

		Days.									
No.	Sex.	9	10.	11.	12.	14.	16.	17.	18.	19.	20
1.	F.	1.0	1.0	1.2	0.7	1.0	1.1	0.6	---	1.0	0.7
2.	M.	0.8	0.9	1.3	0.7	---	0.6	1.2	1.4	0.9	0.7
3.	M.	0.8	1.0	1.1	0.6	1.1	1.0	1.2	0.8	1.1	1.0
4.	M.	---	---	---	---	---	0.8	1.3	1.1	0.7	0.5
5.	F.	0.9	1.0	1.1	---	1.2	1.0	1.2	1.1	0.9	0.6
6.	F.	1.0	0.9	1.1	1.0	1.2	0.9	0.4	0.7	0.7	0.5
7.	M.	0.8	1.5	0.9	1.0	0.7	1.0	1.2	1.4	1.0	1.1
8.	M.	0.7	1.0	1.2	0.5	0.7	1.0	0.8	0.7	0.7	0.8
9.	M.	0.7	1.4	0.9	1.0	1.2	1.1	0.9	0.9	1.1	0.5
10.	M.	0.4	0.8	---	0.8	1.2	1.1	0.9	0.9	0.9	0.6
11.	M.	0.4	1.2	0.9	0.6	0.9	1.4	0.7	0.9	0.7	0.6
12.	M.	0.7	1.1	1.1	0.8	1.1	1.4	1.0	0.7	1.0	1.0
13.	F.	---	---	---	---	0.8	0.9	0.8	1.0	1.0	1.0
14.	F.	---	---	---	---	1.1	0.7	1.3	1.3	---	0.9

		Days.									
No.	Sex.	21.	23.	24.	25.	26.	27.	30.	31.	32.	33.
1.	F.	0.9	1.1	0.8	1.0	1.3	0.8	0.6	0.7	1.3	0.7
2.	M.	1.2	1.3	0.9	0.7	1.1	1.7	1.0	0.9	1.2	1.0
3.	M.	1.0	1.1	1.3	0.8	0.6	1.0	0.7	1.6	---	1.1
4.	M.	1.1	1.1	0.9	0.7	1.0	0.7	0.9	0.8	1.2	1.7
5.	F.	0.7	1.1	1.0	0.9	0.5	1.0	1.0	0.9	1.4	0.7
6.	F.	0.9	1.2	1.4	1.4	1.1	0.9	1.4	1.2	1.1	1.4
7.	M.	0.8	1.6	1.0	1.2	1.1	1.1	1.2	---	1.4	1.6
8.	M.	1.2	1.3	1.3	---	0.9	0.9	1.0	1.4	1.9	---
9.	M.	1.0	1.1	0.8	1.3	1.4	1.0	1.2	1.1	1.3	1.5
10.	M.	1.1	1.0	1.0	1.2	1.6	1.0	1.0	1.3	2.1	1.2
11.	M.	1.1	1.3	0.9	1.1	1.2	0.9	1.0	1.1	1.3	1.4
12.	M.	1.3	1.4	1.5	1.2	1.4	1.0	1.3	1.1	1.1	1.0
13.	F.	0.8	1.4	1.5	1.5	1.5	1.5	1.8	1.4	2.2	1.4
14.	F.	1.2	0.7	1.2	1.2	1.3	0.8	1.4	0.9	1.2	1.2

		Days.									
No.	Sex.	34.	35.	37.	39.	41.	42.	44.	45.	46.	47.
1.	F.	1.0	1.2	1.0	0.8	0.8	0.9	0.9	1.3	0.8	0.9
2.	M.	0.8	1.0	1.1	---	0.6	1.3	0.9	0.8	1.0	0.8
3.	M.	1.2	1.4	1.1	---	0.8	1.9	0.7	1.0	0.8	1.3
4.	M.	0.6	1.1	0.9	---	0.5	1.2	1.1	0.8	1.1	0.6
5.	F.	1.1	1.4	0.9	---	0.5	1.1	1.4	1.3	1.0	0.8
6.	F.	0.8	1.2	0.8	---	0.8	1.1	---	1.0	0.8	1.0
7.	M.	---	1.1	0.6	---	---	2.3	1.3	1.0	1.0	1.5
8.	M.	1.1	1.5	1.1	---	0.4	1.0	0.9	1.1	1.1	0.9
9.	M.	1.0	0.8	1.0	---	0.6	1.5	---	0.9	0.8	1.0
10.	M.	0.6	1.1	0.8	---	0.6	1.1	0.7	1.1	0.7	0.6
11.	M.	1.0	1.4	0.8	---	0.6	1.0	1.2	0.9	1.1	1.0
12.	M.	1.4	---	1.0	---	1.0	2.0	0.9	---	0.9	0.9
13.	F.	1.1	1.7	0.8	---	0.7	1.4	1.3	0.9	0.8	1.5
14.	F.	1.2	1.1	1.4	---	1.1	1.1	1.0	0.9	0.9	0.9
15.	M.	---	---	---	---	---	---	---	---	0.9	---

No.	Sex.	Days. 48.	51.	52.	53.	54.	55.	56.	58.	59.	60.
1.	F.	1.4	1.0	0.9	0.8	1.3	1.6	2.0	2.0	1.5	1.3
2.	M.	0.9	1.1	1.0	0.9	1.6	1.4	0.6	0.8	1.2	1.1
3.	M.	1.3	0.8	1.0	1.0	1.2	1.0	1.0	1.3	1.0	1.4
4.	M.	0.8	0.8	0.5	1.1	1.0	1.1	1.3	1.2	1.0	1.2
5.	F.	1.1	0.9	0.8	0.9	1.2	---	1.0	1.3	1.0	---
6.	F.	1.1	1.0	1.2	0.8	2.0	1.1	0.7	1.4	0.9	1.1
7.	M.	1.1	---	1.4	1.3	1.6	2.2	1.6	1.4	1.3	---
8.	M.	1.0	1.0	1.0	0.7	1.3	1.0	1.0	0.8	1.0	1.7
9.	M.	1.1	0.6	1.0	---	1.3	1.0	0.7	1.3	1.0	1.3
10.	M.	0.8	1.0	1.1	1.0	1.0	0.8	0.7	1.6	0.8	1.5
11.	M.	1.5	1.0	1.2	0.9	1.3	1.4	1.2	1.0	0.9	1.4
12.	M.	1.0	---	---	0.9	1.6	1.1	1.5	1.2	1.4	1.6
13.	F.	1.5	1.0	0.9	1.0	1.4	1.1	1.7	1.6	0.8	1.4
14.	F.	1.4	1.0	0.9	1.0	1.7	1.6	2.0	1.4	1.0	1.2
15.	M.	0.7	0.7	0.7	1.4	1.6	1.3	1.3	1.6	1.0	1.1

		Days.									
No.	Sex.	61.	62.	63.	65.	66.	67.	68.	69.	70.	72.
1:	F.	1.0	1.4	1.3	1.0	1.0	1.0	1.3	1.5	0.8	1.2
2.	M.	---	1.1	1.7	1.3	0.6	1.0	1.0	1.5	1.1	1.1
3.	M.	1.3	0.7	0.6	0.8	1.0	0.9	1.0	1.2	1.0	1.4
4.	M.	1.1	0.9	1.2	1.0	0.5	0.7	1.1	1.3	0.9	1.2
5.	F.	1.5	1.0	1.3	1.6	1.2	0.9	1.3	1.0	1.2	0.7
6.	F.	1.5	1.3	1.2	0.9	1.0	1.2	1.3	2.1	1.1	0.9
7.	M.	1.5	1.4	1.6	1.0	1.7	1.3	1.7	---	1.3	1.5
8.	M.	1.0	0.8	0.5	0.9	1.2	1.2	1.3	1.2	0.8	---
9.	M.	1.4	---	1.4	1.4	0.7	0.9	1.1	1.0	0.7	1.3
10.	M.	1.2	0.8	1.0	1.6	0.6	0.8	1.4	---	0.9	1.0
11.	M.	1.4	1.0	---	1.3	1.5	1.0	1.2	1.6	1.2	1.3
12.	M.	1.9	1.3	0.7	1.3	1.4	1.4	1.4	1.6	---	1.3
13.	F.	1.5	0.9	1.0	1.0	1.2	2.3	1.1	1.1	1.5	1.1
14.	F.	1.1	1.5	1.2	1.3	2.1	1.2	1.6	1.0	1.0	1.5
15.	M.	1.1	1.2	1.7	1.2	1.4	1.4	1.0	1.5	1.1	1.3

		Days.									
No.	Sex.	73.	74.	75.	76.	77.	84.	85.	86.	87.	88.
1.	F.	1.6	0.8	---	1.1	0.6	---	---	---	---	2.0
2.	M.	1.2	1.9	---	1.0	0.8	---	---	---	---	1.0
3.	M.	1.5	1.5	---	0.8	1.1	---	---	---	---	1.1
4.	M.	1.6	1.5	---	---	---	1.1	0.6	---	---	---
5.	F.	---	0.7	---	---	---	---	---	1.1	0.7	1.8
6.	F.	1.2	1.6	---	---	1.5	---	---	---	---	---
7.	M.	1.6	1.4	---	---	---	0.9	---	---	---	---
8.	M.	1.2	2.0	---	1.3	0.8	---	---	---	---	---
9.	M.	1.6	1.3	---	---	1.2	---	---	---	---	---
10.	M.	1.4	1.6	---	---	1.3	---	---	---	---	---
11.	M.	---	---	---	---	---	1.1	0.6	---	---	---
12.	M.	1.6	---	1.5	1.1	---	---	---	---	1.1	2.1
13.	F.	1.5	---	---	---	---	---	---	1.4	0.8	1.8
14.	F.	1.5	---	---	---	0.9	---	---	---	---	---
15.	M.	1.2	---	1.5	0.8	---	---	---	---	---	---

		Days.									
No.	Sex.	89.	90.	91.	95.	96.	97.	98.	102.	103.	104.
1.	F.	1.2	---	---	---	---	---	---	1.0	---	---
2.	M.	0.8	---	---	---	---	---	---	---	---	---
3.	M.	1.1	---	---	---	---	---	---	---	---	---
4.	M.	---	---	---	1.3	0.6	---	---	1.4	---	1.1
5.	F.	---	---	---	---	---	0.8	1.1	---	---	0.9
6.	F.	---	___	---	---	---	---	---	1.4	---	0.8
7.	M.	---	---	---	---	---	1.0	1.5	1.6	---	0.9
8.	M.	1.5	0.6	---	---	---	---	---	---	---	---
9.	M.	---	___	0.7	---	---	---	---	1.8	---	---
10.	M.	---	---	0.8	1.1	1.0	---	---	1.8	---	0.8
11.	M.	---	---	---	1.4	1.0	---	---	1.4	---	1.4
12.	M.	---	---	---	---	---	1.1	1.1	2.0	---	0.9
13.	F.	---	___	0.8	---	---	1.7	---	2.1	---	1.4
14.	F.	---	___	1.3	---	---	---	---	---	---	---
15.	M.	1.2	0.6	---	---	---	---	1.3	1.6	---	1.4

		Days									
No.	Sex.	105.	106.	107.	108.	109.	110.	111.	113.	114.	115.
1.	F.	1.0	1.0	0.8	1.0	1.6	1.8	1.0	0.9	0.8	0.9
2.	M.	1.5	1.1	1.1	1.4	1.5	1.4	1.0	1.2	1.5	1.0
3.	M.	---	1.2	0.9	1.0	1.5	1.1	0.7	---	1.4	1.2
4.	M.	1.6	1.0	1.3	1.2	1.0 *	0.6	0.7	---	1.3	1.0
5.	F.	1.5	1.0	0.9	0.8	0.8	1.4	0.7	---	1.0	1.1
6.	F.	---	1.4	1.1	0.8	2.4	1.4	0.9	---	1.3	1.4
7.	M.	0.8	1.1	1.4	0.7	1.6	1.6	1.2	---	1.7	1.4
8.	M.	---	---	1.3	1.1	1.6	1.8	1.3	1.2	1.0	0.6
9.	M.	---	---	---	2.0	2.0	1.0	0.6	1.0	1.0	0.8
10.	M.	1.4	---	0.9	2.0	1.7	---	1.5	0.8	1.0	1.3
11.	M.	1.2	0.9	1.0	1.4	1.6	---	1.3	1.1	0.8	0.6
12.	M.	1.4	1.6	0.8	1.8	1.7	1.2	0.8	---	1.1	0.8
13.	F.	2.0	1.1	1.5	1.8	1.7	1.3	0.8	---	0.9	0.9
14.	F.	---	---	0.7	1.1	2.1	1.7	1.5	0.8	0.8	0.8
15.	M.	1.4	1.7	1.0							

* 1/750 Milligram Tuberculin (T.R.)

		Days.									
No.	Sex.	116.	117.	118.	120.	122.	123.	124.	127.	128.	129.
1.	F.	0.9	0.8	0.8	0.8	---	---	1.0	---	0.8	1.5
2.	M.	1.2	1.5	---	0.9	1.0	1.0	---	0.6	---	0.8
3.	M.	---	1.0	---	0.8	0.8	1.1	1.0	---	0.8	1.2
4.	M.	---	0.8	---	---	---	---	1.0	---	---	---
5.	F.	---	1.3	---	0.8	---	---	1.1	0.9	---	1.3
6.	F.	---	0.9	---	1.0	---	---	---	1.0	---	0.6
7.	M.	---	1.0	---	0.9	---	---	1.2	1.3	---	0.6
8.	M.	1.2	0.4	0.8	0.8	1.1	1.0	---	---	---	0.6
9.	M.	---	0.9	---	---	---	---	1.1	---	---	0.7
10.	M.	1.2	0.6	---	---	---	---	1.0			
11.	M.	1.1	1.2	0.9	1.0	1.4	1.0	---	---	---	0.7
12.	M.	---	0.6	---	1.0	---	---	1.4	---	---	0.8
13.	F.	1.4	1.1	---	---	0.9	0.9	0.8	---	---	---
14.	F.	0.8	0.5	0.7	0.9	1.8	1.4	0.8			
16.	M.	1.0	1.0	1.1	0.6	---	---	1.4	1.0	---	---

		Days.									
No.	Sex.	130.	131.	132.	134.	135.	136.	137.	138.	141.	142.
1.	F.	0.6	---	0.9	---	1.5	1.2	---	---	0.9	0.8
2.	M.	1.2	1.2	---	---	0.6	1.3	---	1.5	0.8	0.8
3.	M.	1.4	1.1	---	---	1.7	---	---	0.8	0.7	0.9
4.	M.	1.3	---	---	---	1.4	---	---	---	0.8	---
5.	F.	1.3	---	0.7	---	1.3	1.3	---	---	0.8	1.0
6.	F.	0.9	---	1.1	---	---	---	---	---	---	---
7.	M.	0.9	0.8	---	0.9	1.5	1.1	---	1.1	0.7	0.9
8.	M.	0.9	---	1.0	0.7	1.3	1.0	---	1.0	0.8	1.1
11	M.	1.2	0.8	---	1.1	---	1.1	1.4	---	0.4	---
12.	M.	1.2	---	1.0	---	0.9	1.3	1.7	---	---	---
13.	F.	0.9	---	0.7	---	1.3	1.2	0.8	1.0	0.9	1.2
16.	M.	1.4	1.1	---	—	0.8	1.5	1.3	1.2	0.5	1.7
17.	M.	0.7	0.4	---	---	0.8	0.9	1.2	1.0	0.8	1.5
18.	M.	1.2	---	1.0	—	0.8	0.6	0.8	1.0	0.5	1.0
19.	M.	1.0	---	0.8	0.9	---	---	---	---	0.5	---

		Days.									
No.	Sex.	143.	144.	145.	148.	149.	150	151.	152.	153.	154.
1.	F.	0.7	1.2	1.1	0.9	0.9	1.0	0.8	0.8	---	0.8
2.	M.	1.1	0.9	0.6	---	0.6	0.8	0.6	---	---	0.8
3.	M.	1.3	1.3	0.8	---	1.1	1.0	1.0	1.1	0.9	1.0
4.	M.	1.4	0.7	1.3	---	0.9	1.0	1.4	1.6	0.8	0.5
5.	F.	0.9	0.8	1.5	0.7	0.8	0.8	1.1	1.0	1.1	0.7
6.	F.	1.1	1.2	0.5	1.1	0.9	---	0.8	1.0	1.1	0.8
7.	M.	1.1	1.3	0.5	---	0.9	0.8	0.7	0.8	1.0	---
8.	M.	0.8	1.4	0.8	1.0	1.3	0.9	1.1	1.1	1.1	1.0
11.	M.	1.2	1.0	1.6	1.7	0.9	0.8				
12.	M.	---	1.4	1.1	---	1.0	---	1.0	1.1	---	0.6
13.	F.	1.4	1.5	1.1	---	0.9	0.9	1.2	1.0	1.0	0.7
16.	M.	1.2	1.0	1.1	---	1.2	---	0.8	1.1	0.9	1.0
17.	M.	1.2	1.0	0.9	---	0.8	0.9	1.5	1.5	---	0.9
18.	M.	0.8	1.1	1.1	---	1.3	1.1	---	1.3	1.3	---
19.	M.	0.8	1.2	1.3	---	0.8	1.1	0.9	1.0	1.6	0.7

		Days.									
No.	Sex.	155.	156.	157.	158.	159.	161.	162.	163.	164.	168.
1.	F.	1.0	0.6	0.9	1.0	0.8	0.8	0.9	1.3	1.1	---
2.	M.	1.3	0.8	0.9	0.9	0.7	1.0	1.1	1.6	0.7	1.7
3.	M.	1.1	1.1	0.9	1.0	0.8	0.9	1.3	1.1	1.2	1.0
4.	M.	1.4	0.5	0.8	0.9	0.8	1.1	1.1	1.0	0.7	---
5.	F.	1.0	0.8	1.0	1.0	0.8	0.9	1.0	---	1.7	1.2
6.	F.	1.0	0.9	1.3	1.1	1.2	0.8	1.2	1.3	1.0	1.0
7.	M.	---	---	1.1	---	0.8	0.8	1.1	1.4	1.2	1.7
8.	M.	0.9	0.7	0.9	0.8	1.1	1.3	1.3	1.7	1.0	0.8
12.	M.	0.8	0.8	1.0	1.2	1.1 0.9	0.6	1.0	1.4	1.4	0.9
13.	F.	0.9	0.8	1.2	0.6	0.9	0.8	1.2	1.1	---	0.9
16.	M.	1.3	0.9	1.1	1.4	1.6	0.9	1.6	1.5	1.1	1.1
17.	M.	0.6	0.7	0.8	1.2	1.5	1.3	1.5	1.9	1.3	1.1
18.	M.	1.3	0.7	1.2	0.7	---	1.4	1.2	1.3	1.0	Haemoptysis
19.	M.	0.5	0.9	1.3	---	1.0	1.1	1.1	1.8	1.1	---

		Days.									
No.	Sex.	169.	170.	171.	172.	173.	175.	176.	177.	178.	179.
1.	F.	1.1	0.75.	0.8	1.4	---	1.4	1.2	0.9	1.9	1.1
2.	M.	1.5	1.5	1.1	1.6	1.5	1.2	0.5	1.3	---	1.3
3.	M.	1.0	---	---	---	1.6	1.2	0.9	0.7	---	1.3
4.	M.	1.5	0.9	1.1	0.8	1.0	1.2	0.8	1.0	---	0.8
5.	F.	1.0	1.1	1.1	1.4	1.0	0.7	0.8	1.4	1.6	1.1
6.	F.	1.1	1.0	1.0	0.9	1.2	1.2	0.9	1.1	1.2	0.8
7.	M.	0.9	1.1	1.1	1.1	1.1	1.1	1.0	0.9	1.9	1.0
8.	M.	1.3	1.2	0.8	1.1	1.0	1.2	0.8	0.7	0.9	1.0
12.	M.	0.9	0.8	1.0	1.0	1.3	1.3	1.2	---	1.2	1.0
13.	F.	0.7	0.8	0.8	0.9	0.9	1.1	0.5	0.7	0.9	0.7
16.	M.	2.0	1.1	0.8	0.7	1.5	1.0	1.6	1.2	1.4	1.6
17.	M.	1.0	0.7	0.8	1.0	1.2	1.2	1.3	1.1	---	1.2
18.	M.	---	1.1	---	1.1	1.1	---	---	---	1.5	0.9
19.	M.	0.8	0.8	1.0	0.8	1.5	---	0.6	0.6	1.3	0.6

No.	Sex.	Days. 180.	182.	183.	184.	185.	186.	189.	191.	192.	193.
1.	F.	0.9	0.9	1.0	0.9	0.7	0.7	1.1	1.2	1.0	1.3
2.	M.	1.1	1.1	1.4	1.3	1.1	1.7	0.7	1.6	0.9	1.2
3.	M.	1.3	0.9	1.2	0.9						
4.	M.	1.0	1.3	1.0	1.05.	1.1	1.0	1.0	1.3	0.8	0.8
5.	F.	1.6	---	0.9	1.5	0.9	1.4	1.4	1.4		
6.	F.	0.7	1.0	1.0	1.0	1.0	1.0	0.9	1.2		
7.	M.	0.9	1.2	1.3	1.3	0.9	0.8	1.3	1.2	0.7	0.8
8.	M.	---	1.0	1.1	1.0	1.0	1.0	1.1	1.1	0.9	1.1
12.	M.	1.2	1.1	1.5	1.6	0.8	0.7	0.7	1.0	0.8	1.0
13.	F.	0.8	1.2	1.1	0.9	0.8	0.8	1.0	0.8	0.9	0.8
16.	M.	1.6	1.1	1.4	1.8	0.9	1.0	0.7	0.9	1.1	---
17.	M.	0.8	0.7	1.1	1.0	0.9	0.7	0.9	1.2	0.8	0.8
18.	M.	0.9	1.2	1.7	1.5	1.1	1.0	1.2	1.1	0.9	1.1
19.	M.	0.8	1.0	1.1	2.0	1.2	1.3	0.6	1.5	1.2	1.2

INDIVIDUAL CASES.

The particular cases which I wish to refer to specially may be divided into three groups.

1st. Early cases which seem to have benefited by tuberculin treatment, comprising numbers 1,8,12,15,16,20 and 21; and case No. 19 on account of the interest attaching to it from a diagnostic point of view.

2nd. Long-standing cases which have gained some benefit from the treatment, namely, Nos. 2, 4, 13, and 22.

3rd. Cases which have not benefited to any degree by the treatment, cases No. 14, and 23.

Case No.1.

Female, age 25, has had a cough as long as she can remember, becoming worse lately; haemoptysis in May 1904 and again in Feby. 1905; at the age of 20 had an attack of pneu-:monia, and at 24 had a severe attack of bronchitis.

Family history. No history of phthisis.

Diagnosis. Right apical lesion, early infiltration; signs slight, very little moisture, occasional crepitations at the base from the bronchial element.

Height. 5feet 3 inches.

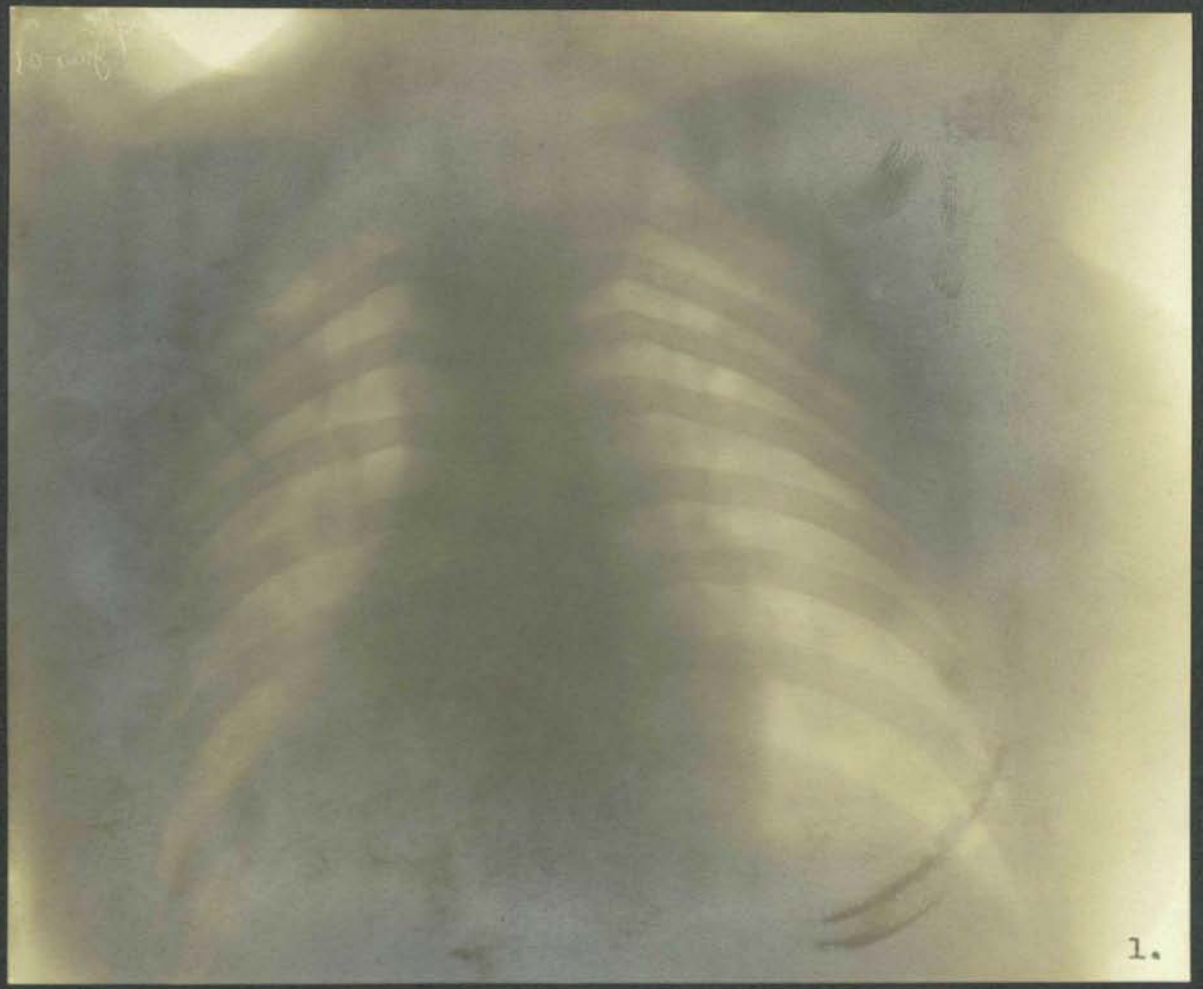
Weight on admission, 55.900 kilos.

Average maximum temperature 37 C.

Average minimum temperature 36.5 C.

The record of opsonic indices and doses of tuberculin follow and are continued under Case No. 1 in the Tables.

This case is doing well and is chiefly of interest because of the few physical signs and also because tubercle bacilli could not be demonstrated in the sputum for a long time after the patient came under treatment. The evidence of the opsonic index and the negative phase after inoculation with tuberculin was ultimately confirmed by tubercle bacilli being found in the sputum at a later date.


1.

DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.	DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.
1.		0.8	27.		1.1
2.		1.0	29.		1.5
3.		1.0	30.		1.0
4.		1.1	31.		0.7
5.	1/500 mg.	0.8	32.		1.0
6.		0.7	33.	1/500 mg.	1.4
8.		0.5	34.		1.3
9.		0.6	36.		1.2
11.		1.4	37.		0.9
12.		1.0	38.		1.1
13.		2.3	39.		1.0
15.		1.2	40.		0.8
16.	1/500 mg.	1.6	41.		1.1
18.		1.2	43.		1.0
19.		1.6	44.		1.6
20.		2.3	45.		1.1
22.		0.9	47.		1.2
23.		1.0	48.		1.2
24.		0.8	49.		1.0
25.		0.7	50.		0.6
26.		1.1	51.		0.8

Case No. 8.

Male, age 29, suffered from an attack of pleurisy in December 1904, and in March 1905 haemoptysis occurred.

Family history. Two brothers died of phthisis at ages 17 and 21.

Diagnosis. Early infiltration of the right upper lobe and, doubtful, very early infiltration of the right lower lobe.Unmixed infection.

Height. 5 feet 9 inches.

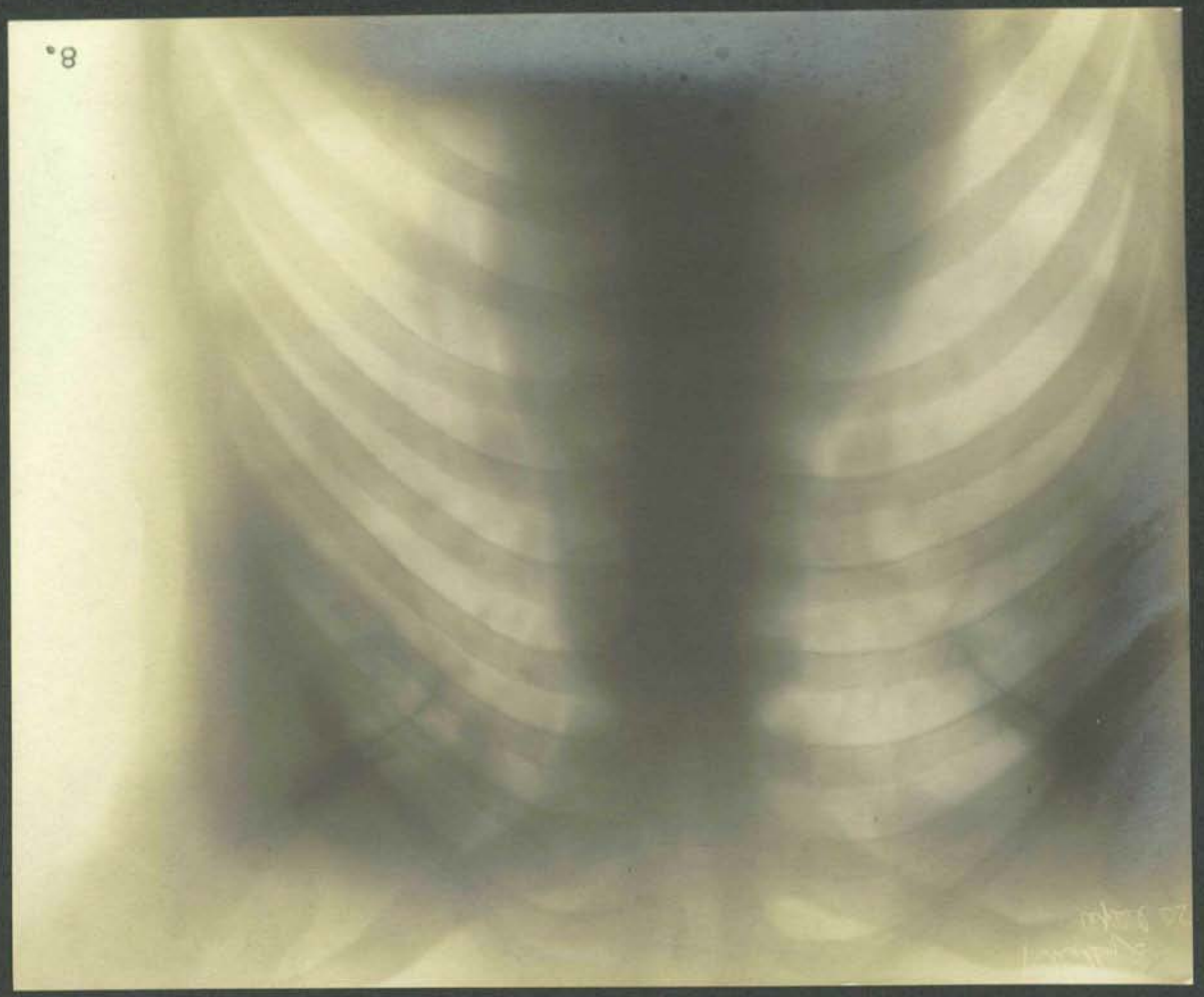
Weight on admission. 66.800 kilos.

Average maximum temperature. 37 C.

Average minimum temperature 36.5 C.

Record of opsonic indices in the Tables under Case No. 8.

This case is practically cured. There are no tubercle cacilli and almost no sputum. The opsonic index is at the normal standard, and is almost steady.


8

Case No.12.

A well-developed male, age 25, in May 1904 had tinged sputum, and in June tubercle bacilli were found. He entered Pinewood Sanatorium, where he remained till February 1905. During that time he had small haemor-:rhages repeatedly. After February 1905 he spent four months at home, but on account of the recurrence of haemoptysis was advised sanatorium treatment again, and entered Nordrach-on- Dee July 1905.

Family history. One sister age 21 died of phthisis.

Diagnosis. Physical signs on admission, infiltration with a few scattered medium rales to the sixth dorsal spine behind and to the septum in front, with moisture (scattered rales) to the third rib on the right side; signs of an arrested lesion on the left side. No excavation.

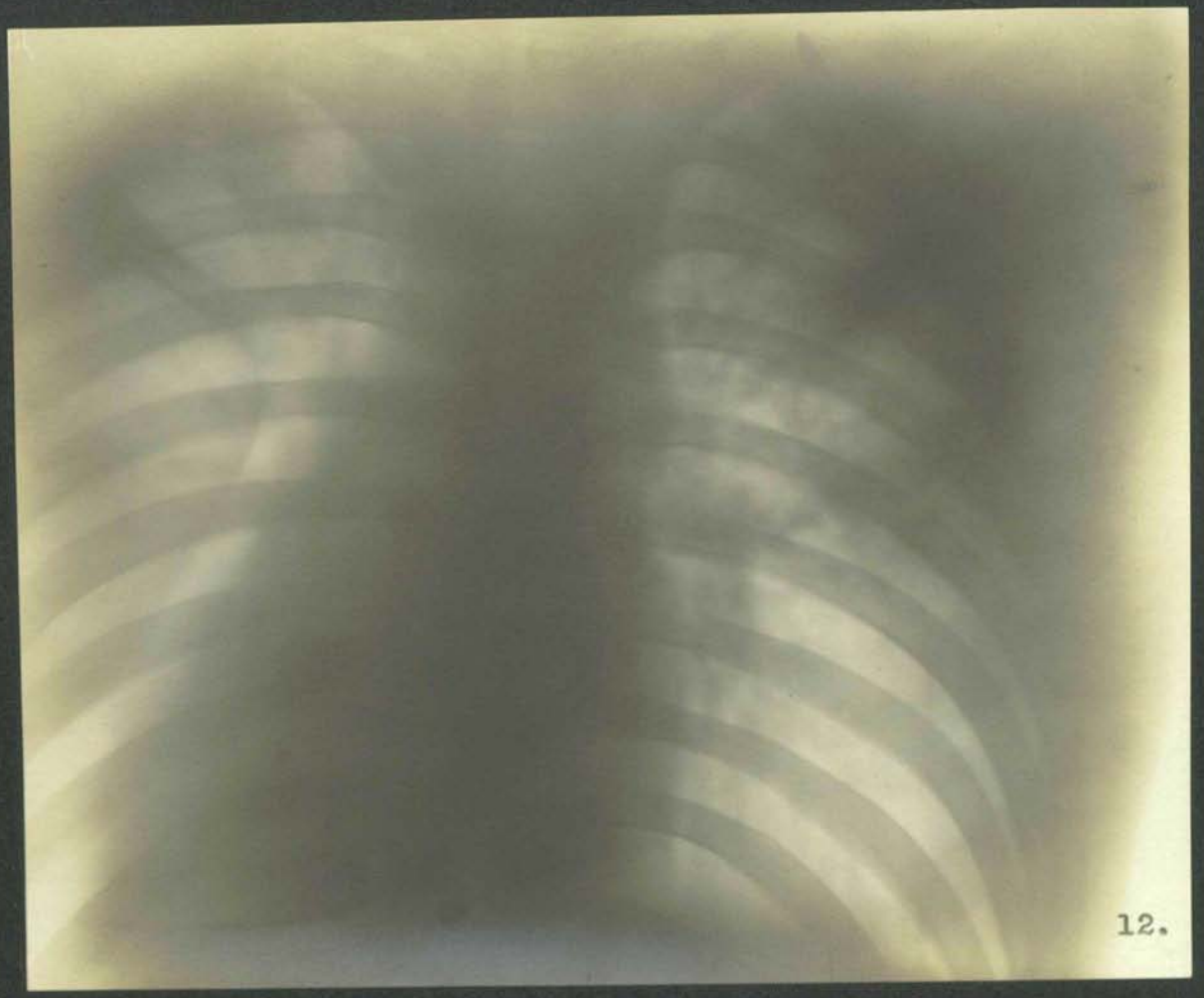
Height 6 feet 1 inch

Weight on admission. 72.800 kilos.

Temperature range at the time inoculations were begun 36.9 to 37.5 C.

Weight. 73.950 Kilos.

Record of opsonicindices under Case No.12. in the Tables.



12.

This case is doing well. The sputum is reduced almost to a trace, and although repeatedly examined during the last month no tubercle bacilli have been found; staphylococci are fairly abundant indicating staphylococcus vaccine treatment.

Present weight. 72.650 kilos.

Temperature range. 36.6 to 37.1 C.

Case No.15.

A well-developed male, age 22. In April 1905 had a "cold" with cough and spit, and on the 29th of the same month had a small haemor-:rhage. Nothing was found in the lungs, but tubercle bacilli were found in the sputum. At the age of 16, patient had an attack of double pneumonia.

Family history. Good.

Diagnosis. The case was found to be one of early infiltration of both apices, and possibly also very early infiltration of the right lower lobe, with haemoptysis.

Height. 5 feet 9 inches.

Weight on admission. 63.100 kilos.

Weight at beginning of inoculations 67.000 kilos.

Weight on discharge. 66.700 kilos.

Average maximum temperature. 36.9 C.

Average minimum temperature. 36.5 C.

Record of opsonicindices under case No 15 in the Tables.

This case was practically cured by ordinary sanatorium treatment, but the opsonic index being found to remain low, tuberculin treatment was advised and adopted in order to raise the opsonic index before discharge.

CASE No. 16.

Male, age 22, has suffered from asthma and hay fever occasionaly during the last four years. The present illness began as a "cold on the chest" with a small amount of sputum.

Family history. Father died of pulmonary tuberculosis six months ago and one brother dies of same disease eighteen months ago.

Diagnosis. Early infiltration of the right apex. No haemoptysis.

Height. 5 feet 8 inches.

Weight. 63.200 kilos.

Temperature range. 36.6 to 37.3 C.

When tuberculin treatment was started the weight was 65.600 kilos and temperature range 36.6 to 37.1 C.

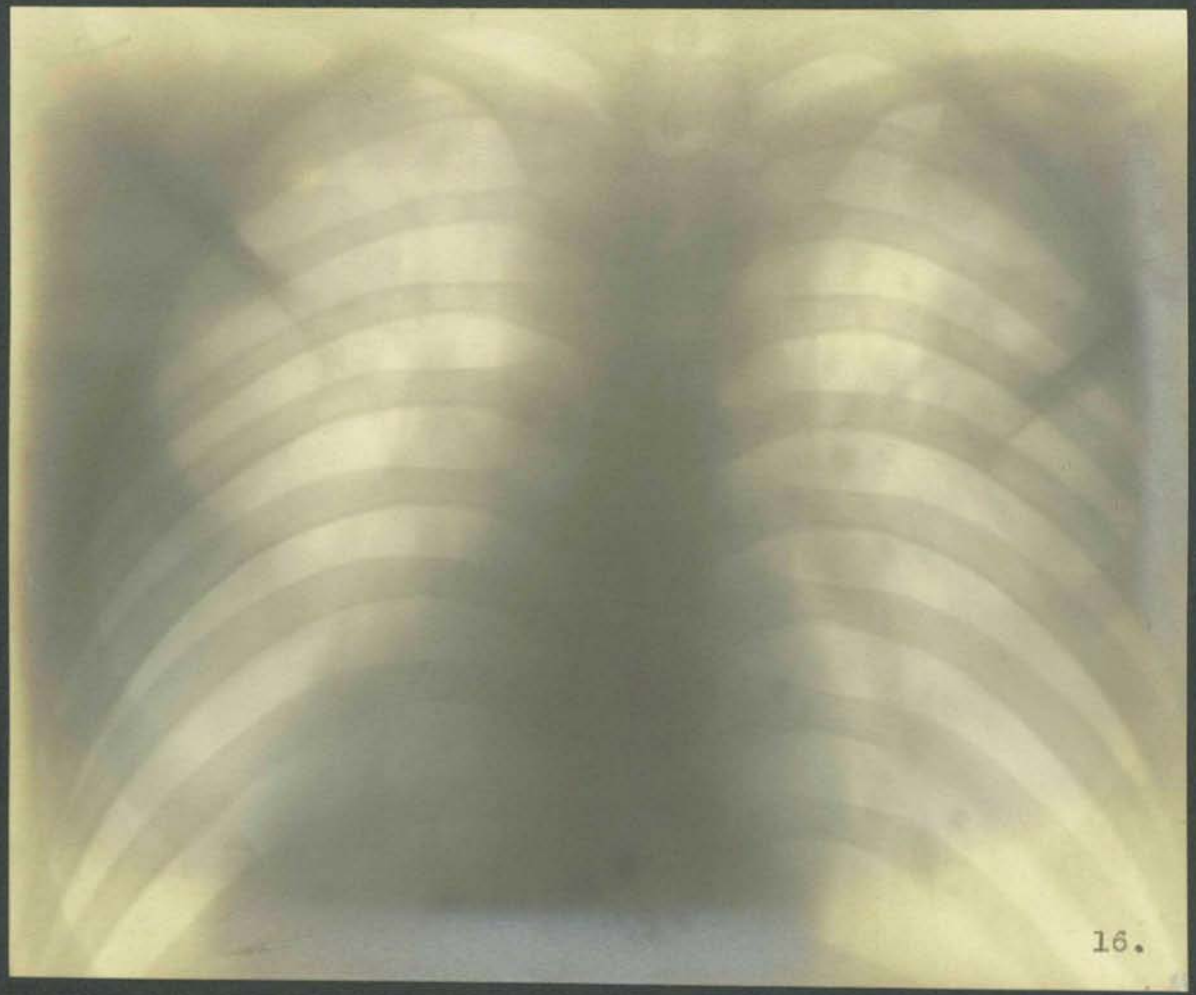
After 3 months combined sanatorium and tuberculin treatment.

Weight was. 68.460 kilos.

Temperature range. 36.1 to 36.9 C.

Sputum. None.

The record of opsonic indices is to be found under Case 16 in the Tables.



16.

Case No.20.

Male age 44, complained of cough and loss of weight. Duration four to five months.

Family history. Good.

Diagnosis. Early infiltration, 2 lobed lesion of the right side,

Under ordinary sanatorium treatment for a year this patient did well in every respect, but tubercle bacilli persisted in considerable numbers in the sputum. Tuberculin treatment was started and the record of opsonic indices is given below. As the presence of tubercle bacilli in the sputum was the chief criterion in this case, careful examination of the sputum was made from time. On the 28th day of the treatment the bacilli were found to be very few in number, and on the 48th day no bacilli could be found, and the sputum has remained free from bacilli from that time.

The opsonic index has been taken at long intervals and although this man leads a very active city life his index has always been found either steadily above or within normal limits.


20.

DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.
1.		0.6
2.		0.6
3.		0.6
4.	1/500 mg.	0.4
5.		0.2
6.		0.3
7.		0.9
8.		0.9
9.		0.9
10.	1/500 mg.	0.8
11.		0.5
12.		0.6
13.		0.6
14.		0.5
15.		0.6
16.		0.7
17.		0.7
18.		1.1
19.		1.0
20.	1/500 mg.	0.8
21.		0.5
23.		0.8
24.		0.8
25.		0.7
26.		0.8
27.		1.5
28.		0.9
30.		1.1
32.	1/500 mg.	0.8
33.		0.6
34.		0.5
35.		0.9
37.		0.8
38.		1.2
39.		0.7
40.		0.7
41.		0.8
42.		0.8
44.		0.9
45.		0.8
46.	1/400 mg.	1.8
47.		0.6
49.		1.0
50.		1.4
51.		0.9
52.		1.2
53.		1.0
54.		1.4
55.		0.9
56.	1/400 mg.	—

DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.
57.		1.3
58.		0.7
59.		1.2
60.		0.8
61.		1.1
62.		1.0
64.		1.0
65.		1.0
66.		0.7
67.		0.9
68.		1.1
71.		0.9
72.	1/250 mg.	1.4
73.		0.8
74.		0.8
75.		0.6
80.		0.9
81.		0.7
85.	1/500 mg.	1.3
100.		1.5
115.		1.2
117.		1.4
118.		0.9
121.		1.0
122.		1.7
126.		1.2
128.		1.8
129.	1/250 mg.	—
133.		0.7
135.		1.4
137.		1.3
138.		1.7
149.		1.4
151.		1.6
156.		1.2
158.		1.5
163.		1.4
165.		1.5
8th month		1.2
9th "		1.4
10th "		1.4
11th. "		1.2
13th. "		1.0

Case No.21.

Male age 36. For a long time this patient had been troubled with bronchitis, and went to South Africa on that account. Three years ago in Egypt he had an attack of dysentery followed soon afterwards by an attack of malaria. After returning to this country he suffered frequently from "colds" and began to have a large amount of sputum which latterly was mixed with blood.

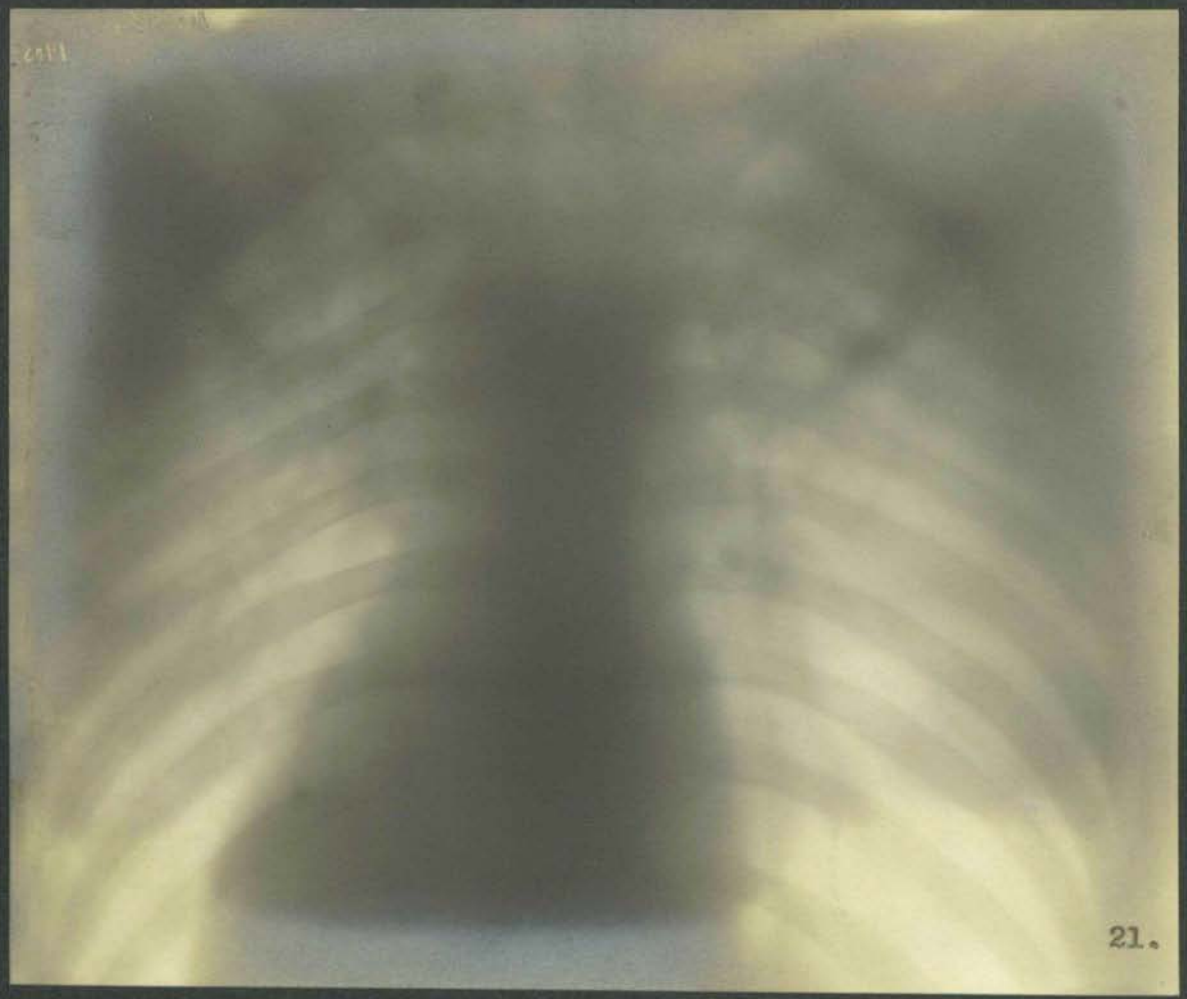
Diagnosis. Bilateral subacute disease, 3 lobed lesion, right upper and lower lobes with left upper lobe. Complication, ischio-:rectal abscess.

Height 5 feet 10 inches.

Weight on admission. 61.750 kilos.

Temperature range. 36.9 to 37.5 C.

Sanatorium treatment was carried on for nine months, during which time the patient's weight increased to 67 kilos, then fell to 63.800 kilos. The range of temperature was 36.9 to 37.4 C. and tubercle bacilli were still abundant in the sputum. The physical signs in the lungs had improved and altogether the patient was much better. Tuberculin was at this point added to the ordinary treatment and the record of opsonic indices follows.



Weight. Steady at 63.800 kilos.

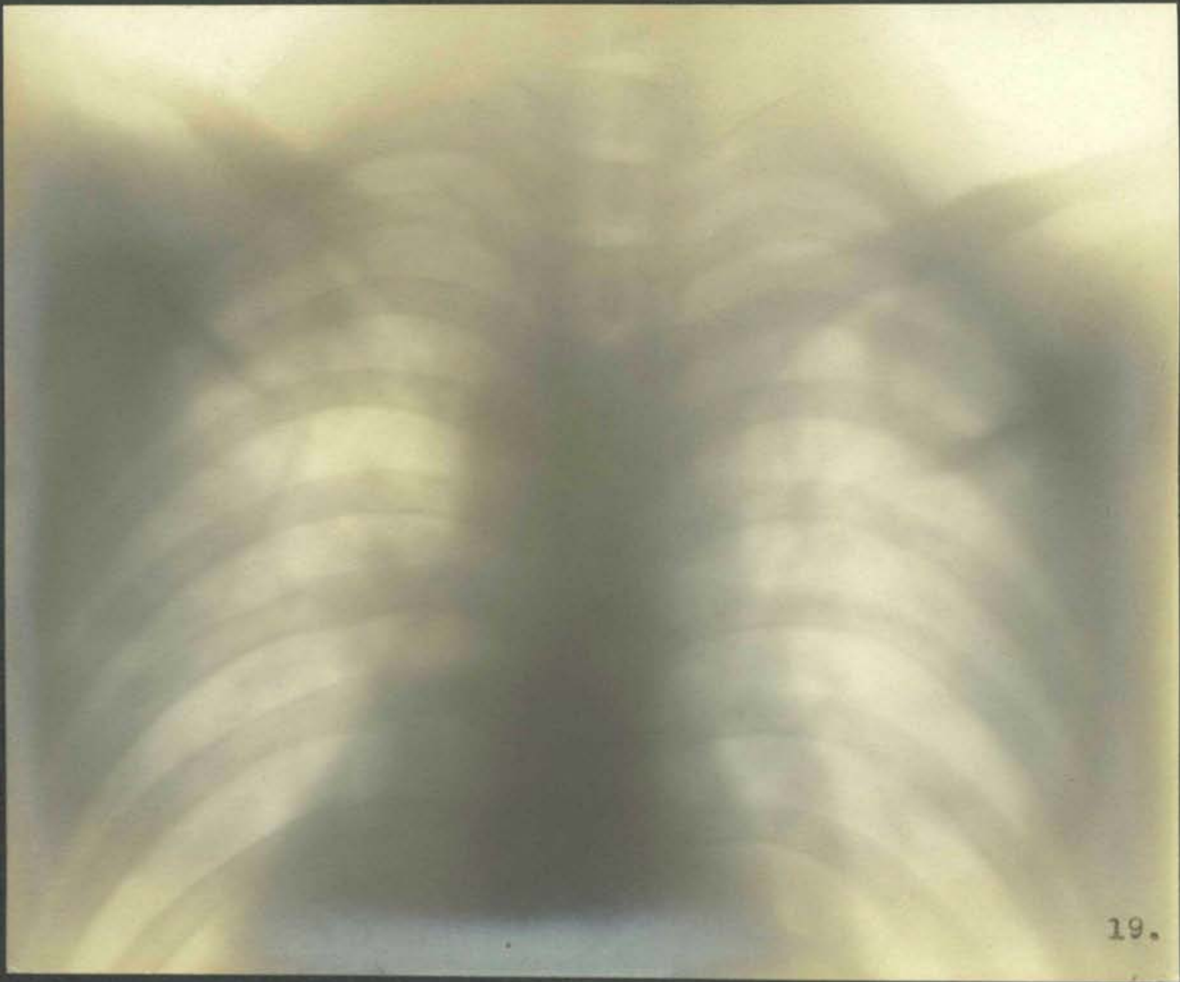
Temperature range. 36.4 to 37.2 C.

Tubercle bacilli disappeared from the sputum and ultimately there was no sputum.

DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.	DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.
1.		0.6	67.		0.5
7.		0.7	70.		0.9
11.	1/500 mg.	0.9	71.		0.8
12.		0.4	72.		1.3
13.		0.8	73.		0.8
14.		0.9	74.		1.0
15.		0.9	75.		1.1
16.		0.7	77.		0.6
17.		1.1	78.		1.1
18.		0.8	79.	1/500 mg.	1.5
19.	1/500 mg.	0.9	80.		0.3
21.		0.8	81.		1.1
22.		0.7	82.		1.6
23.		1.3	84.		0.9
24.		1.1	86.		0.7
25.		1.4	97.		0.7
26.		1.4	88.	1/500 mg,	1.5
28.		0.6	89.		1.0
29.		0.8	91.		1.3
30.		0.9	92.		0.8
31.		0.7	93.		1.2
32.		0.6	94.		0.7
33.		0.8	95.	1/500 mg.	1.4
35.		0.8	96.		0.4
36.		0.9	98.		0.6
37.		1.1	99.		1.5
38.		1.3	100.		1.5
39.		0.9	105.		0.8
40.		0.9	106.		1.2
42.		1.2	107.		1.1
43.	1/500 mg.	1.3	108.		0.6
44.		0.5	109.		0.5
45.		0.8	112.		1.3
46.		1.8	113.		1.1
47.		1.2	114.		1.0
49.		1.1	115.		1.2
51.	1/500 mg.	1.6	116.		0.8
52.		0.8	117.		0.7
53.		1.1	119.		1.0
54.		1.2	120.		0.8
57.		1.1	121.		0.8
59.		0.9	122.		0.5
60.		0.9	123.	1/250 mg.	1.5
61.		0.9	124.		0.95
63.		0.9	126.		1.0
64.		0.8	127.		1.6
65.		1.0	128.	1/250 mg.	1.0
66.	1/500 mg.	1.5	129.		0.4
			130.		1.8

Case No. 19.

This case already has been referred to on page 62. The case was originally one of early infiltration of the right apex, and after six months sanatorium treatment was considered cured. The opsonic index being found at the lower limit in health after several examinations (0.8, 0.9, 0,7,) it was thought advisable to administer a dose of tuberculin in order to raise the index as in case No. 15. The patient being very desirous to go home was permitted to do so, 1/750th milligram tuberculin (T.R.) being administered there, and unfortunately a daily record of opsonic indices was not made. On the fourth day after inoculation however, a specimen of blood was received which gave a phagocytic index of 1.3, showing that the negative phase had passed. Four daily observations immediately following the last showed a gradually descending opsonic index (1.0, 0.8, 0.9, 0.6); soon afterwards it was learned that the patient had developed an ischio-rectal abscess following an attack of influenza. The abscess was evacuated thoroughly but the tuberculo-opsonic index remained unaccountably low. A few weeks


19.

later the patient was found to have developed mischief in the left apex. The accompanying skiagraph clearly shows a lesion in each apex--that in the right apex, so far as physical signs can be relied on being arrested, that in the left apex, as the history and physical signs show, just beginning. At the time of writing the abscess cavity has almost entirely healed and the patient is also otherwise making good progress, and the prognosis is favourable.

This case is exceedingly interesting in so far as the opsonic index roused suspicion that all was not well in the patient's lungs more than a month before any physical signs could be found to locate the seat of mischief although careful search had been made for such signs. The opsonic observations are continued under case No. 19 in the Tables.

Case No. 2.

Male, age 30, a case of five years duration, tubercle bacilli found in the sputum in February 1901, haemorrhages from time to time, and pleurisy on the right side.

Diagnosis. Unilateral subacute disease, involving three lobes on the right side, with considerable bronchial involvement; moisture heard down to the base, medium rales; bronchial element prominent.

Height. 5 feet 11 inches.

Weight. (June 1905) 77.560 kilos.

Sputum. Average 45 c.cs.

Temperature at the beginning of tuber-:culin inoculations 36.5 to 37.4 C.

Improvements. Weight increased to 82.700 kilos; temperature reduced to 36.5 to 36.9 C. sputum reduced to 5 to 10 c.cs.

Record of opsonic indices under case No. 2 in the Tables.


2.

Case No. 4.

A male, age 42, mining engineer in various parts of the world, has had repeated attacks of malaria, and left-sided pleurisy for the last twenty years. Pneumonia on the left side accompanied by haemorrhage at the end of 1902. The patient comes of a large family with no history of phthisis.

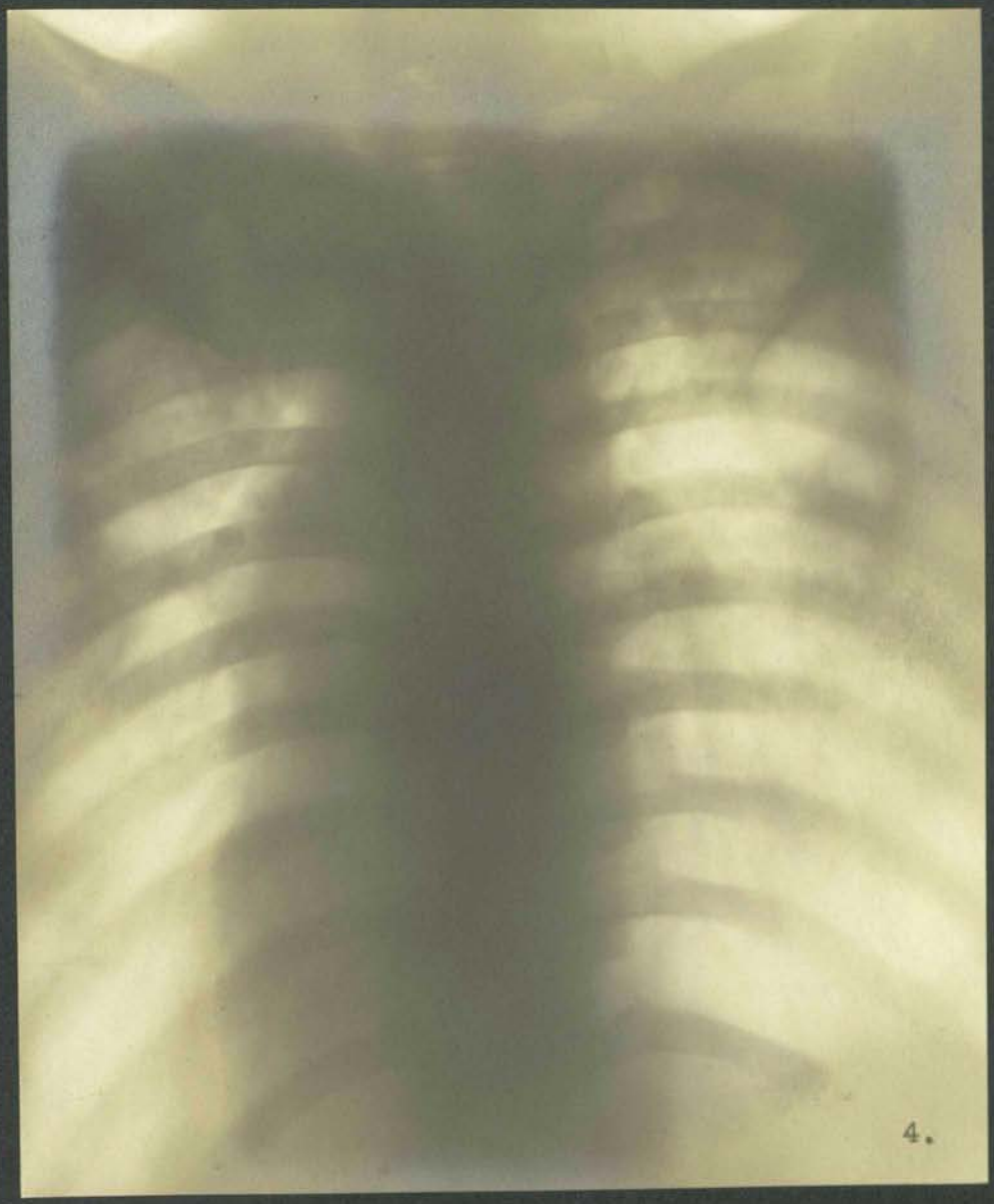
Diagnosis. The case is one of chronic progressive disease, 4 lobed lesion, left side the worse; some emphysema, no excavation.

Height. 5 feet 9 inches.

Weight on admission. 51.100 kilos.

The prognosis on entrance was as follows: with the long duration of the disease, extensive distribution, poor general health, and after repeated attacks of malaria prognosis is not favourable.

After prolonged sanatorium treatment tuberculin was begun in February 1905, and the record of his opsonic indices follows. When the patient was started on tuberculin treatment his weight was 61.650 kilos, sputum was fairly copious, tubercle bacilli abundant, and dyspnoea marked. Temperature range 36.2 to 37 C.



4.

At the present time the weight is 64.400 kilos; sputum, a trace containing no tubercle bacilli but considerable numbers of staphylococci for which staphylococcus vaccine is at present being administered. The dyspnoea in also greatly inproved, and the patient can walk moderate distances without the previously severe effort.

Weight at present. 64.400 kilos

Temperature range. 36.5 to 37 C.

In this case the dose of tuberculin varies from 1/50th to 1/2000th milligram. A dose of 1/500th milligram was given at first and by an error 1/50th milligram was administered later in the treatment. No ill effects followed and a dose of 1/250th milligram was used for some time afterwards.

DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.	DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.
1.		0.6	58.		0.8
2.	1/500 mg.	0.7	59.		0.6
3.		0.4	62.	1/500 mg.	1.3
4.		0.8	63.		0.5
5.		0.9	64.		1.1
6.		0.8	65.		0.7
7.		0.8	66.		1.0
8.		0.8	67.		1.1
9.		1.0	69.		0.9
10.		1.0	70.	1/500 mg.	1.4
11.		0.7	71.		0.9
13.		0.9	72.		0.8
14.	1/500 mg.	1.2	73.		0.8
15.		0.6	74.		1.0
16.		0.5	76.		1.1
17.		0.9	78.		1.2
18.		1.6	79.		0.9
20.		1.8	80.		1.2
21.		0.9	81.		1.1
22.	1/500 mg.	1.1	83.		1.1
23.		0.8	84.		0.9
24.		1.0	85.	1/500 mg.	1.8
25.		0.9	86.		0.7
27.		1.0	87.		1.1
28.		1.3	88.		1.5
29.		1.3	89.		0.7
30.	1/500 mg.	1.4	90.		1.1
31.		0.7	91.		1.3
32.		1.3	96.		1.0
34.	1/500 mg.	2.05.	97.		1.3
35.		0.9	98.		0.8
36.		1.7	99.	1/50 mg.	1.2
37.		1.1	100.		0.9
38.		2.5	103.		0.9
39.		1.2	104.		0.9
41.		1.1	105.		1.1
42.		1.0	107.		0.8
43.		1.7	108	1/250 mg.	1.6
44.		0.8	109.		0.7
45.		0.8	110.		1.3
46.		1.2	111.		1.2
48.		1.1	112.	1/250 mg.	1.8
49.		1.0	113.		0.9
50.		0.8	114.		1.0
51.		1.0	116.		0.9
52.		1.2	118.	1/250 mg	1.4
53.		1.1	119.		0.8
55.		1.1	120.		0.9
56.	1/500 mg.	1.3	121.		1.0
57.		0.6	123.		0.7

DAY.	DOSE OF TUBERCULIN.	OPSONIC INDEX.
124.	1/250 mg.	1.7
125.		0.5
126.		0.8
127.		0.9
128.		1.1
130.		0.5
131.		1.2
133.		1.2
134.		1.3
135.		0.9
136.		1.7
140.		1.5
141.		1.1
143.		1.1
144.		0.9
145.		1.0
146.	1/250 mg.	1.3
147.		0.4
148.		1.3

The opsonic indices are continued under Case No. 4 in the Tables.

This case is of especial interest in as much as the dosage was varied throughout the treatment and the inoculations were made at the highest points in the positive phases in order if possible to obtain a greater therapeutic effect and a greater immunising result.

Case No. 13.

Female, age 27, well-developed and tall, old-standing case. At the age of nineteen she had a haemorrhage. She has always lived in healthy surroundings in the country.

Family history. Patient comes of a large family, no other member of which has ever shown any sign of phthisis; an aunt, however, died of phthisis. Patient had a governess in whose room the patient slept, and who died of pthtisis: this is a probable source of infection in this case.

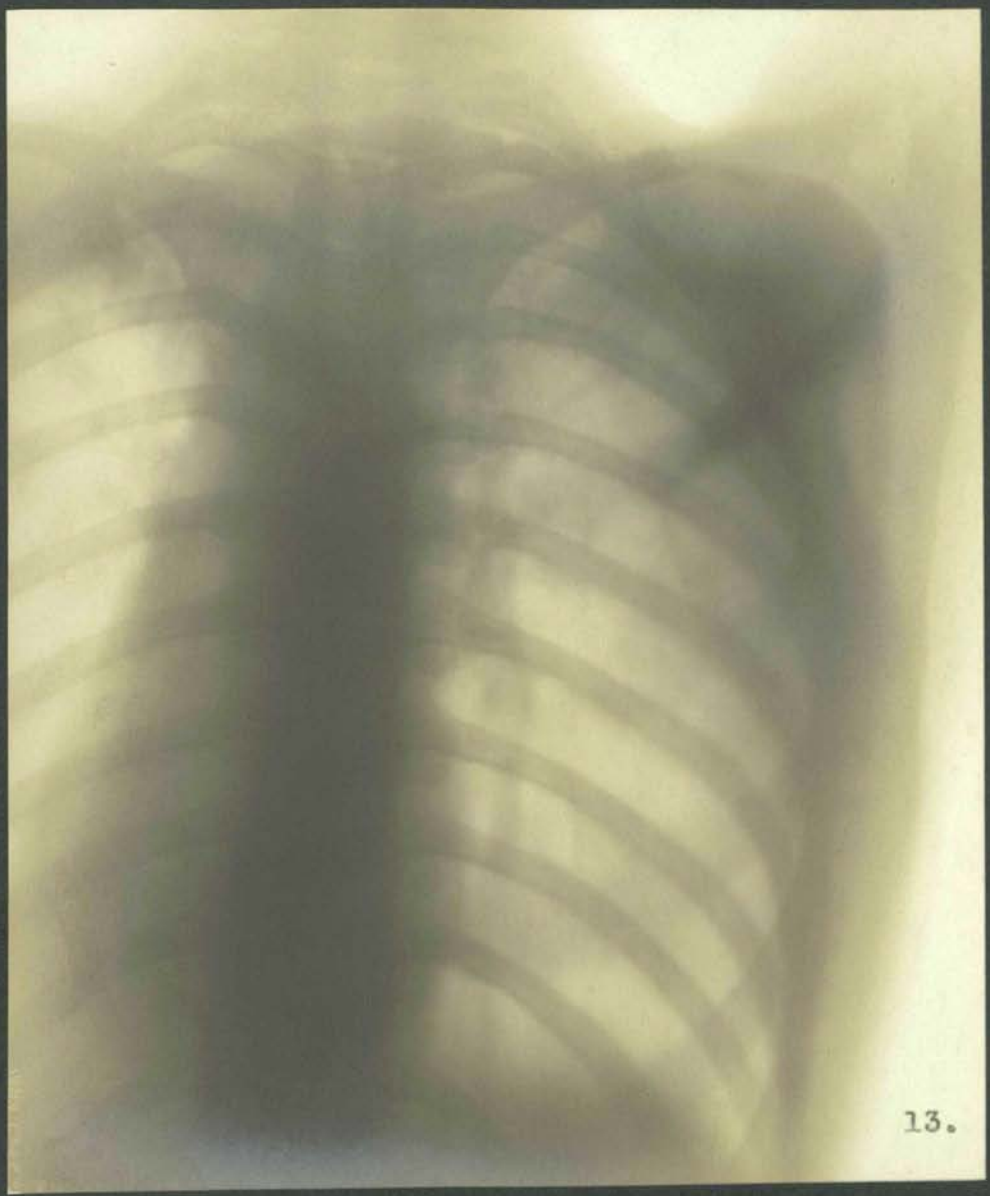
Diagnosis. Chronic fibroid, 3 lobed lesion, left upper and lower lobes with early disease in the right upper lobe; probably a little excavation. Mixed infection. Duration eight years.

Height 6 feet 1 inch.

Weight on admission. 63.400 kilos.

Pyrexia on admission, temperature range 37 to 37.6 C. Sputum about 40 to 70 c.cs. Tubercle bacilli numerous.

After prolonged sanatorium treatment during which there was an increase in weight, but temperature range the same and an increase in sputum to 75 to 140 c.cs. the patient was put on tuberculin treatment.



13.

The improvements since tuberculin was started are:- slight increase in weight, reduction of temperature 36.6 to 37.1 C., reduction in amount of sputum to 40 c.cs, and disappearance of tubercle bacilli from the sputum, although staphylococci are fairly numerous. Record of opsonic indices under Case No. 13 in the Tables.

Case No.22.

Male, age 57, had a cough for a long time which was always worse in winter. Three years ago physical signs of phthisis were discovered. At the age of 37 he contracted syphilis, and at 40 had an attack of pleurisy. The family history doesnot give any indication of phthisis.

Diagnosis. Chronic fibroid, 4 lobed lesion, cavity formation and enlarged bronchial glands at the root.

The patient had two years sanatorium treatment before tuberculin treatment was tried. When the latter wasstarted the weight was 71.000 kilos, temperature range 36.6 to 37.3 C. and sputum 65 c.c..

As will be seen in the record of opsonic indices following, the dose of tuberculin was at first 1/500 milligram reduced later to 1/1000 milligram. The tuberculin treatment extended over a year and at the middle of that term the weight was 73.600 kilos, the temperature range 36.6 to 37.2 C., and the sputum about the same amount as before. What is of chief interest is that tubercle bacilli disappeared from the sputum

while tuberculin treatment was being carried on.

Weight on discharge. 72.800 kilos.

Temperature range. 36.4 to 37.2 C.

Sputum. Same amount, no tubercle bacilli.

Two and a half months after tuberculin treatment was stopped tubercle bacilli were again found in the sputum.

DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.	DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.
1.		0.5	66.		0.6
2.		0.8	67.	1/500 mg.	1.1
4.	1/500 mg.	1.1	69.		1.0
6.		0.6	70.		0.6
7.		0.9	71.		1.6
8.		1.0	72.		0.9
9.		0.7	73.		0.9
10.		1.3	74.		0.8
11.	1/500 mg.	1.3	75.		1.3
12.		1.0	76.		1.1
13.		0.9	77.		0.9
14.		1.0	79.		0.8
15.		1.7	80.		1.5
17.		0.6	81.		1.3
18.		1.4	82.		1.0
19.		1.1	83.		1.5
24.		1.8	84.	1/500 mg.	1.3
25.		1.6	85.		0.5
26.	1/500 mg.	1.2	86.		1.0
27.		0.9	87.		1.0
28.		0.8	88.		1.0
29.		1.0	89.		0.8
32.		1.2	90.		0.9
33.		1.4	92.		1.0
34.		1.3	93.		1.8
35.	1/500 mg.	1.3	94.		1.0
36.		0.6	96.	1/500 mg.	1.6
38.		1.8	97.		0.7
39.		1.0	98.		1.0
40.		1.3	99.		1.2
41.		1.5	100.		1.2
43.		1.3	102.		1.3
45.		1.2	105.		1.4
46.		1.6	106.	1/1000 mg.	1.6
47.		1.4	107.		0.7
48.		1.0	108.		1.1
49.		1.9	109.		1.0
50.		0.9	111.		1.1
52.		1.1	112.		0.6
53.	1/250 mg.	1.3	113.		1.1
54.		0.7	114.		0.8
55.		0.9	115.		2.1
56.		0.7	116.		0.8
57.		1.5	118.	1/1000 mg.	1.0
59.		0.6	119.		0.5
60		1.2	120.		0.9
62.		0.9	121		1.0
63.		0.7	122.		1.3
64.		0.7	123.		1.1

DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.
125.		0.8
127.	1/1000mg.	0.9
128.		0.7
149.		1.3
150.		1.3
151.		0.9
153.		0.8
154.		1.1
155.		1.3
156.		0.8
190.		0.5
192.		0.5
193.		1.0
195.		1.1
196.	1/1000 mg.	0.8
197.		0.7
198.		0.8
199.		1.2
202.		0.9
203.		1.1
204.		1.0
205.		1.1
206.		1.3
207.		1.2
209.	1/1000 mg.	1.1
210.		1.0
211.		1.5
212.		0.8
213.		0.7
214.		1.5
216.		1.4
217.	1/1000 mg	1.0
218.		0.7
219.		0.9
220.		1.4
221.		0.8
223.		0.4
224.		1.5
225.		0.8
235.	1/1000 mg.	0.8
236.		0.7
246.	1/1000 mg	1.3
247.		1.1
258.		1.1
260.	1/1000 mg.	0.8
261..		1.1
262.		1.2
263.		0.8
265.		1.5

Case No. 14.

Female, age 26, had haemoptysis in Australia in 1902. Marmorek's serum was tried but without effect. Larynx involved. First seen in May 1905.

Diagnosis. Fibro-caseous disease of the left upper and lower lobes which has definitely extended to involve the right side; excavation present and extending in both lobes in the left side. The case is really one of 5 lobed lesion.

Height 5 feet 6½ inches.

Weight on admission. 60.580 kilos.

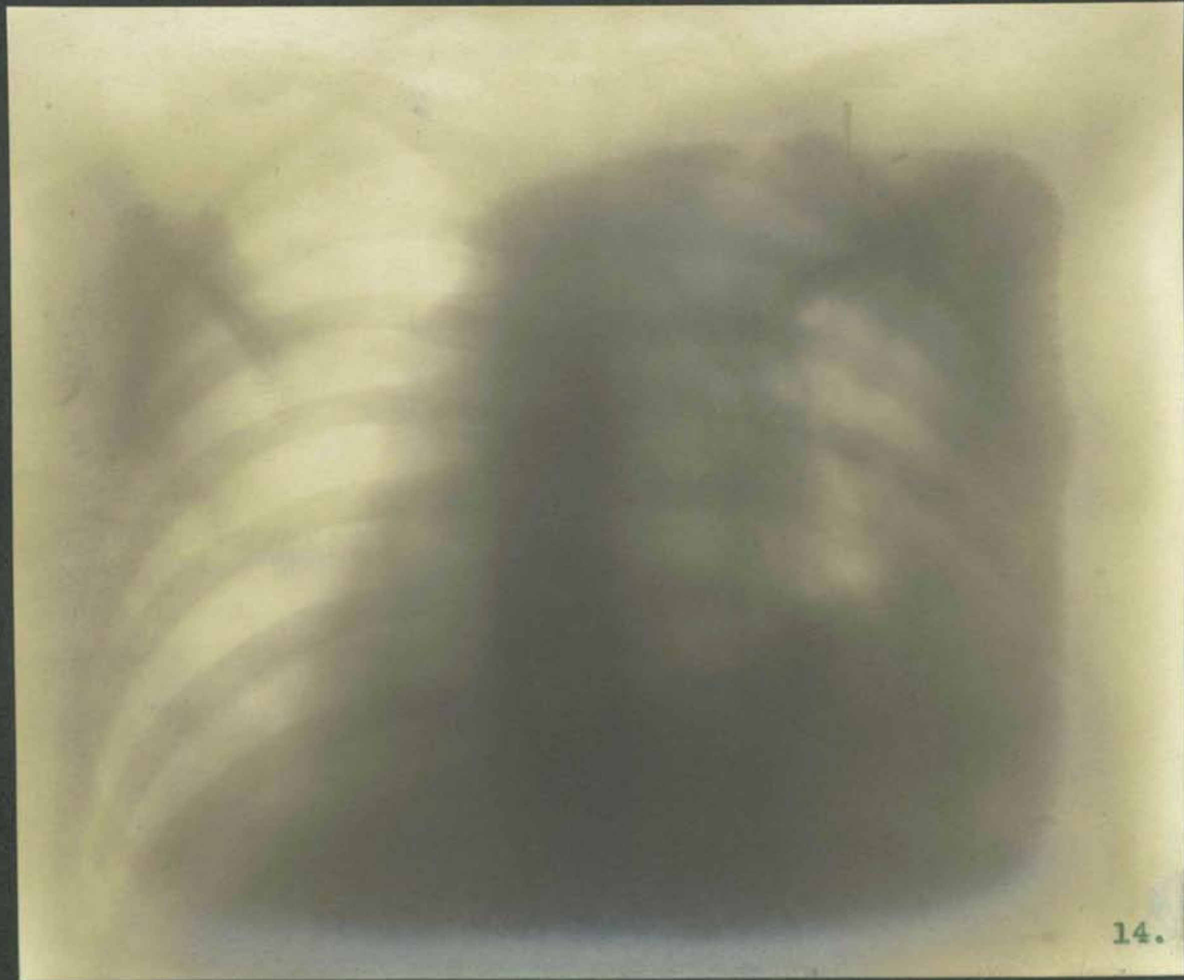
Temperature range. 36.9 to 37.9 C.

Tuberculin treatment started October 1905. Present weight 67.200 kilos.

Temperature range. 37 to 38.6 C.

As this case was doing badly and the inoculations were seen to be of no value, tuberculin treatment was stopped.

Record of opsonic indices under Case No. 14 in the Tables.



14.

Case No. 23.

Female, age 23. Early in 1902 she began to cough, and had an attack of shingles in the left side. Later in the same year she suffered from neuralgia in the back between the shoulders. Afterwards the voice became hoarse and continued so to the end.

Family history contains no indication of phthisis, all the members being alive and healthy except one brother who died as the result of an accident.

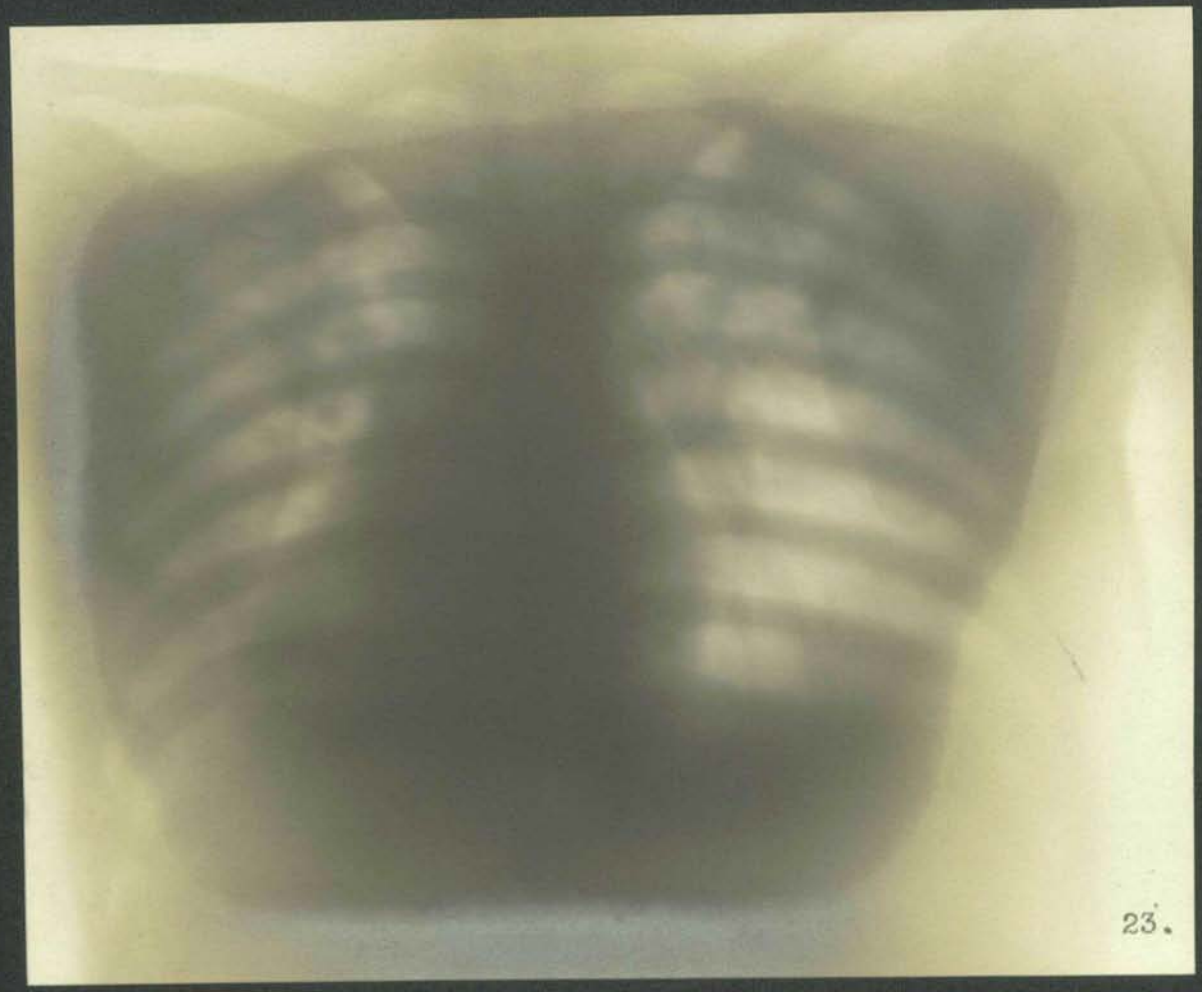
Diagnosis. Fibro-caseous disease, bilateral, excavation well-marked. Spinal caries (fourth to sixth dorsal vertebrae) which improved with rest, but the disease on the whole extended.

Weight on admission. 51.100 kilos.

Temperature range. 37 to 37.5 C.

After nearly two years sanatorial regime, although not looked upon as a suitable or hope-:ful case tuberculin was tried for a time, and at the beginning of the treatment the weight was 52.600 kilos, temperature range 36.8 to 37.6 C., sputum 55 c.c..

Within two weeks of death the weight was still the same and the temperature range 36.9 to 38 C. The opsonic index was taken till within two weeks of the end, and the record



follows. For several weeks tuberculin was not administered. Later two doses were given but the treatment was discontinued as being of no value in this case.

DAY.	DOSE of TUBERCULIN.	OPSONIC INDEX.
1.		0.5
3.		0.6
4.		0.7
5.		0.8
6.		1.0
7.		0.6
8.		1.0
10.		1.6
11.		0.5
12.		0.6
13.		0.6
14.		0.7
15.		0.8
17.		0.8
18.		1.0
19.		0.9
20.		0.9
21.		0.8
22.		0.7
24.		0.6
25.		1.3
26.		1.0
27.		1.1
28.		1.1
29.		0.6
30.		0.9
32.		0.8
33.		1.1
34.		0.6
35.		0.7
36.		0.6
38.		0.8
39.		1.0
40.		0.6
411.		0.5
42.		0.9
43.		0.8
46.		1.0
88.	1/500 mg.	0.9
89.		0.8
92.		1.0
93.		0.6
95.		1.2
96.		1.1
98.		0.9
99.		0.9
100.		0.8
102.		0.6
105.		1.0
106.		0.6
107.		0.7
108.		0.5
110.		1.0
113.		1.1
114.		1.1
115.		1.2
116.	1/1000 mg.	1.0
117.		1.0
118.		0.7
120.		0.9
121.		0.7
122.		0.8
123.		0.7
124.		0.9
125.		0.9
127.		0.7
128.		0.5
129.		0.5
130.		0.6
131.		0.6
132.		1.1
136.		0.6
137.		0.9
158.		1.0
159.		0.6
160.		0.9
162.		1.0
163.		0.6
164.		0.5
165.		0.7
166.		0.6
167.		0.7
169.		0.9
170.		0.7
171.		0.7